

L12 I

QUANTITATIVE ASSESSMENT OF
CARDIAC FUNCTION IN DOGS
USING THE APEXCARDIOGRAM

FREDA MARION SCOTT-PARK

PhD
UNIVERSITY OF EDINBURGH
1985



CONTENTS

Acknowledgements	i
------------------------	---

Abstract	ii
----------------	----

SECTION ONE : INTRODUCTION AND REVIEW OF LITERATURE

1.1	Introduction	1
1.2	Apexcardiography	2
1.3	The Genesis of Apical Impulses	5
1.4	Correlation of Physiologic with Abnormal Configuration ..	10
1.5	The Concept of Myocardial Contractility	12
1.6	Quantification of Data from the ACG	16
1.7	Systolic Time Intervals	18
1.8	Physiological Correlation with STI	20
1.9	The Effect of Heart Rate and Cycle change on STI	22
1.10	Use of the Apexcardiogram to obtain STI	24
1.11	Clinical Application of STI	27
1.11.1	Myocardial Disease	30
1.11.2	Valvular Disease	30
1.11.3	Aortic Stenosis	31
1.11.4	Pericardial Disease	31
1.11.5	Conduction Defects	32
1.11.6	Dysrhythmias	32
1.12	Aims of this Study	33

SECTION TWO : EARLY EXPLORATIVE WORK

2.1	<u>Introduction</u>	34
2.2	<u>Materials and Methods</u>	35
2.2.1	Experimental Preparation	35
2.2.2	Recording Equipment	35
2.2.3	Recording Technique	37
2.3	<u>Results</u>	43
2.4	<u>Discussion</u>	57
2.5	<u>Conclusions</u>	61

SECTION THREE : CALCULATION OF SYSTOLIC TIME INTERVALS USING THE
APEXCARDIOGRAM

3.1	<u>Introduction</u>	62
3.2	<u>Materials and Methods</u>	64
3.2.1	Anaesthetic Procedure	64
3.2.2	Recording Technique	64
3.2.3	Recording Procedure in Conscious Dogs	65
3.2.4	Analysis of Simultaneous Recordings	65
3.2.5	Division of Dogs into Groups	68
3.3	<u>Results</u>	69
3.3.1	Data from Group A Dogs	69
3.3.2	Data from Group B Dogs	76
3.3.3	Data from Group C Dogs	86
3.4	<u>Discussion</u>	100
3.4.1	Recording Equipment	100
	Preamplifiers	
	Transducers	
	Final Amplifiers	
3.4.2	The Use of Anaesthesia	103
3.4.3	Limitations of Apexcardiography in Measurement of STI ...	104
3.4.4	Discussion of Results and Comparison with other Studies .	106
3.4.5	Effect of Myocardial Ischaemia on STI	109

SECTION FOUR : SYSTOLIC TIME INTERVALS FROM THE APEXCARDIOGRAM IN
DOGS WITH HEART DISEASE

4.1	<u>Introduction</u>	111
4.2	<u>Materials and Methods</u>	112
4.2.1	Recording Procedure	112
4.2.2	Calculation of STI Indices	115
4.3	<u>Results</u>	119
4.3.1	Reasons for Poor Quality Apexcardiograms	119
4.3.2	Systolic Time Intervals	119
4.3.3	STI Indices	139
4.4	<u>Discussion</u>	145
4.4.1	Recording Procedure	145
4.4.2	Recording of the ACG in Various Breeds	145
4.4.3	Discussion of the Results	147
	Alterations in QS_2	
	Alterations in LVET	
	Alterations in PEP	
	Alterations in PEP/LVET	
4.4.4	Apexcardiography in Clinical Situations	152
4.4.5	The Effect of Drugs on STI	159

SECTION FIVE : GENERAL DISCUSSION, PROJECTED STUDIES AND
CONCLUSIONS

5.1	General Discussion	161
5.2	Projected Studies	164
5.3	Conclusion	167

APPENDICES

Appendix 1 Technical Data for Recording Equipment.....170

Appendix 2 STI Values for all Dogs in this Study173

Appendix 3 Computer Programs182

Appendix 4 Definitions and Abbreviations191

REFERENCES192

TABLE CONTENTS

SECTION TWO

Table 2.1 Details of Dogs	44
---------------------------------	----

SECTION THREE

Table 3.1 STI Regression Data from Group A Dogs	76
Table 3.2 STI Regression Data from Conscious Dogs (Group B) ...	84
Table 3.3 Comparison of STI from Group B Dogs	84
Table 3.4 STI from Anaesthetised Dogs	85
Table 3.5 STI from Group C Dogs (after coronary artery ligation)	93
Table 3.6 Comparison of STI : Group A with Group C	93

SECTION FOUR

Table 4.1 Breeds of Dogs	114
Table 4.2 Details of Referred Cases	117-118
Table 4.3 STI in Dogs with Clinical or Suspected Heart Disease	120
Table 4.4 Comparison between STI (normal dogs and clinical cases)	129
Table 4.5 Comparison of STI between Normal Beagles and Normal Dogs (of various breeds)	129
Table 4.6 Deviations from Normal in Dogs with Pulmonic Stenosis	157

FIGURE CONTENTS

SECTION ONE

Figure 1.1	Normal Apexcardiogram	4
Figure 1.2	Duplicated Normal Apexcardiogram - Points on the ACG	9
Figure 1.3	Basic Types of Apexcardiogram	14
Figure 1.4	Systolic Time Intervals from the carotid arterial Pulse	19
Figure 1.5	Definition of Systolic Time Intervals from the Apexcardiogram	25

SECTION TWO

Figure 2.1	Illustration of a Beagle	36
Figure 2.2	Schematic Diagrams of a Dog's Thorax	39-42
Figure 2.3 -2.6	Variations in Apex Waveform	46-50
Figure 2.3	Right Lateral Recumbency, right side	46
Figure 2.4	Right Lateral Recumbency, left side	47
Figure 2.5	Left Lateral Recumbency, right side	48
Figure 2.6	Left Lateral Recumbency, left side	49-50
Figure 2.7	Distortion of the Apexcardiogram during Respiration	52-53
Figure 2.8	Angulation of the Transducer	54
Figure 2.9	Reproduction of the ACG	55-56

SECTION THREE

Figure 3.1	STI obtained from Group A	71-75
Figure 3.2	Comparison of STI from Group B	78-83
Figure 3.3	STI obtained from Group C	88-92
Figure 3.4-3.6	Composite diagrams of QS_2 , LVET and PEP vs HR	95-99
Figure 3.4	Group A	95
Figure 3.5	Group C	97
Figure 3.6	Group B	99
Figure 3.7	Schematic Representation of the Phases of Ventricular Systole	105

SECTION FOUR

Figure 4.1	STI obtained from Referred Cases	122-126
Figure 4.2	Composite Diagrams of QS_2 , LVET and PEP vs HR ...	128
Figure 4.3	The Effect of Panting on the ACG in the Dog	131
Figure 4.4	Pan-systolic Murmur preventing measurement of the ACG	133
Figure 4.5 & 4.6	Distortion of the ACG in Dysrhythmias	135-136
Figure 4.7	Interference with ACG Frequencies	138
Figure 4.8	Deviations from Normal in QS_2 , LVET, PEP and PEP/LVET	141-144
Figure 4.9	Variations in RR Interval as a Result of Atrial Fibrillation	154

Apart from the help and advice acknowledged in the Preface, this thesis represents the unaided work of the author and was not conducted in collaboration with any other person.

Freda M Scott-Park
BVM+S, MRCVS

June 1985

ACKNOWLEDGEMENTS

Dr P.G.G. Darke for his initiation of the idea and his enthusiastic support and advice.

Dr B.J. Alps for negotiating the financial support for the work and for the practical help and encouragement given.

Syntex Research Centre for financing the research and for providing the necessary facilities within the Pharmacology Department.

Mr C Calder for his practical help and the technical advice on computer analysis of results.

Miss S Chisholm for her willingness to type the manuscript and the skill and speed with which it has been completed.

Mr Harrower for his help with the program required for numerous computations.

Mr J Browning for the loan of computing equipment.

Mrs K Oxley for allowing the use of a room for the completion of this thesis.

Mr and Mrs I Widdowson for supplying quality paper and for additional typing skills.

Dunn and Wilson for binding the copies of this thesis and the skill with which this has been done.

And finally to David, my husband, for his tremendous support and help in getting this work completed.

My thanks are due, not only to the above, but to many others too numerous to mention without whom this thesis could not have been completed.

ABSTRACT

Apexcardiography proved to be a practical, non-invasive method for measuring cardiac function in the dog. Simultaneous recordings of the electrocardiogram, apexcardiogram and phonocardiogram were studied in normal dogs before and after the experimental production of ischaemic heart disease and in naturally-occurring clinical cases of cardiac failure.

Recordings of the apexcardiogram were found to have a variable morphology depending on the site of the transducer on the thorax. The optimum site was over the point of maximum apical impulse, between the 5th and 7th ribs in the majority of dogs.

The apexcardiogram in dogs after experimental production of ischaemic heart disease and in clinical cases demonstrated few deviations from normal. The abnormalities observed in apexcardiograms from human cardiac patients were not consistently recorded in this study. Qualitative information in apexcardiograms alone does not appear to be a reliable guide to cardiac function in dogs.

Simultaneous recordings with ECGs and PCGs provided a temporal relationship which may be used to quantify events of the cardiac cycle. STI were derived and normal values established for both anaesthetised and conscious dogs. The STI in dogs with cardiac malfunction after experimentally-produced ischaemic heart disease showed little deviation from normal.

STI were further derived from dogs with heart failure or sub-clinical heart disease and were obtainable in the majority of clinical cases. A significant prolongation of pre-ejection period often accompanied by a decrease in left ventricular ejection time was observed in those dogs considered to have cardiac failure.

SECTION ONE

INTRODUCTION

AND

REVIEW OF LITERATURE

1.1 Introduction

The aim of this study has been to establish a satisfactory non-invasive method of assessing cardiac function. A major criterion was that the technique should be suitable for use in dogs with heart disease.

Prior to 1950 the main source of information of cardiac events were electrocardiograms, peripheral arterial pulses, heart sounds and radiography, when the latter became readily available. Better knowledge of cardiovascular functions came with the development of techniques for catheterisation. This extended to angiography and cineangiography, necessary for identifying defective circulation due to malformations. Catheterisation also allowed quantitative measurements of cardiac output and ventricular volumes to be made.

Despite the inaccessibility of a large and important part of the cardiovascular system, it is possible to assimilate a comprehensive and accurate analysis of the function of the heart. Methods originally used for recording experimental data have been refined and modified to such a degree that they are used in conscious human patients (Kreulen et al, 1975). Unfortunately, the same techniques are not easily applied to conscious dogs, despite many of the many methods having been developed and used in experimental animals.

In human medicine, adequate non-invasive methods of quantifying cardiac function have long been sought. Some means of "bedside diagnosis" which is quickly accomplished and is repeatable as often as required would be valuable. There is an equal need in veterinary practice.

Non-invasive measurements have been used with some success to predict haemodynamic variables which would otherwise require catheterisation. The comparison of normals with individuals having cardiac abnormalities has yielded useful information for diagnosis and prognosis of cardiac disease states.

With familiarity with equipment, recording and possibly interpretation can be accomplished by a competent technician. The ability to delegate duties is essential to a busy clinician. Unfortunately, no single non-invasive test provides a definite diagnosis of cardiac failure.

The handling of dogs and the performance of any invasive or even mildly painful technique is difficult without either sedation or anaesthesia as a form of restraint. Their application to non-experimental dogs is limited. A satisfactory non-invasive, painless technique was therefore sought for use in clinical cases. Apexcardiography is the technique investigated and applied to healthy experimental dogs and dogs with heart disease in this study.

1.2 Apexcardiography

Apexcardiography is the graphic recording of precordial movements by application of a transducer to the chest wall over the area of the apex beat. These movements are produced by a combination of factors which include: (i) cardiac movements; (ii) changes in volume and consistency of the heart; (iii) pulsation of the great vessels. The basic waveform of the apex beat has several well-defined points which have been fully described by the following authors: Benchimol and Dimond, 1963; Tavel et al, 1965; Tafur, Cohen and Levine, 1964; Gay et al, 1978.

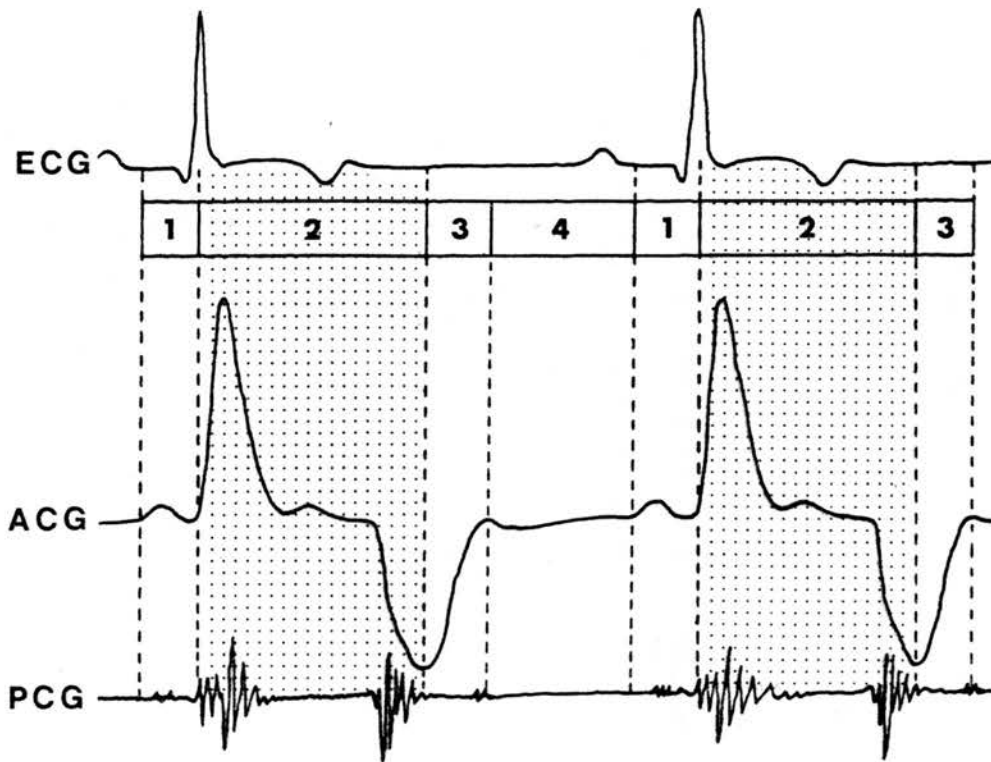
These authors have generally divided the apexcardiogram (ACG) into diastolic and systolic events. In Fig 1.1, phases 1, 3 and 4 represent the diastolic part of the cycle and phase 2 is the systolic component.

The pulsatile phenomena originating from movements of the heart have for long interested physiologists and clinicians. C.H. Parry in 1786 detected oscillations of the trunk synchronous with the heart beat. In 1842 a text book published by James Hope contained descriptions of precordial movements in a variety of disease conditions, an early example of disease helping to define the normal.

In 1877, the first record of the movements of the body, which Parry had previously noticed, was made by Gordon. He published these in a paper entitled "On certain molar movements of the human body produced by the circulation". He compared this motion to the recoil of a gun. Marey in 1885 produced a capsule for picking up the movements at the surface and they were transcribed onto a smoked drum.

These were the beginnings of what are now known as apexcardiography, kinetocardiography (Eddleman et al, 1953 a & b) and ballistocardiography (Mounsey, 1959). These methods have been used to attempt detection of physiologic changes during the cardiac cycle as well as abnormalities of contraction of the diseased ventricle (Benchimol and Dimond, 1963). However, these techniques failed to attain sufficient popularity for them to be widely used until recently. This is partly due to the imprecise nature of the information compared with catheterisation data. Valuable developments within the last two decades have largely eliminated this problem.

Figure 1.1



A Normal Apexcardiogram (ACG) showing the different phases of the waveform and their relationship to the phonocardiogram (PCG) and electrocardiogram (ECG)

Phase 1 = atrial wave

Phase 2 = ventricular systole

Phase 3 = rapid ventricular filling

Phase 4 = slow ventricular filling

The shaded area represents the systolic phase of the cycle.
Recording taken at 100 mm sec⁻¹.

In 1911, Crehore published a paper which was a study of tracings from the region near the apex of the heart. This was prompted by the observation that there was a great difference in the results obtained by placing a transducer in slightly different orientations during recordings in the same person. Crehore's recordings were taken on different days and therefore the pulse rate varies from one tracing to the next. The amplitude varies considerably but the basic shape remains very similar from one recording to another.

The terminology for different parts of the wave does not relate to that used but there are parts of the waveform which are recognisable in Crehore's paper as the wave and the systolic upstroke and ejection period. Crehore calls these the 'presphygmic period' following 'auricular contraction' and 'ventricular systole' respectively. A prominent wave marked "V" was also noted which appears to be what is now known as the rapid filling wave. His conclusion was that the detail to be found in these traces should be of use in both research work and clinical situations.

In the few publications over the next twenty years no attempts were made to correlate ACG findings with physiological events. It was not until the 1950s that interest in the movements of the heart was rekindled (Eddleman et al, 1957). The modern era of investigation of precordial movements probably began with Johnston and Overy's studies published in 1951

1.3 The Genesis of Apical Impulses

The movements over the precordium are complex and difficult to distinguish. One movement, the apex beat, is regular and is ordinarily detectable by palpation. However, its genesis remains obscure (Deliyannis et al, 1964).

It is interesting to note that William Harvey was apparently the first to recognise that the apex beat is a systolic phenomenon. Prior to the publication of his book "De Mortu Cordis" (1628) it had been accepted that this movement was the result of the filling of the heart and therefore occurred in diastole (Eddleman et al, 1957).

The picture is further complicated by the difficulties in interpretation of recordings of the apical impulse. Several workers attempted to define the origins and shape of the apex beat using various recording methods. Eddleman et al (1957) used kinetocardiography and ballistocardiography and published a paper with results from the former; Mounsey (1959) described his recording method as the 'praecordial acceleration cardiogram'. In some instances, the interpretation of normal motions is facilitated by study of certain abnormal states.

Until the early 1960s it was still being argued whether tracings obtained by any method represented recordings of low frequency vibrations or of actual movements of the heart (Johnston and Overy, 1951). Coulshed and Epstein (1963) published a paper which discussed fully the record of low frequency precordial movements. Their conclusions from recording the ACG in normal subjects, were that both movements of the heart and changes in ventricular volume were recorded and the blood flow velocity probably affected the pulse contour.

It is clear that outward movements give rise to an upstroke and inward motion gives a downward deflection (Rios and Massumi, 1965). These movements must reflect changes in ventricular volume.

The morphology of the apexcardiogram is not random; it can be explained on the basis of the known physiological sequence of the cardiac cycle. The cyclic changes in the various dimensions of the ventricles combine to produce alternating expansion and contraction of total ventricular volume (Rushmer, 1976). This motion is recorded in the ACG (see Fig 1.2).

The points of the ACG (Coulshed and Epstein, 1963; Benchimol and Dimond, 1963) are as follows: The A wave is an inconstant feature of the ACG. It follows the P wave of the ECG and is the result of late ventricular filling due to atrial contraction.

Contraction of the atrial muscle reduces the capacity of the atrial chambers and displaces the blood forward into the ventricles. The contraction slightly increases both intra-atrial and intra-ventricular pressures because it suddenly compresses this portion of the venous volume reservoir (Rushmer, 1976). The peak of this wave coincides with the fourth heart sound (S_4) (Benchimol et al, 1961; Tafur et al, 1964).

After the inscription of the A wave the trace develops a rapid positive deflection reaching a maximal systolic peak at the onset of the carotid pulse upstroke (Tafur et al, 1964). This is designated the C-E interval. The C point roughly coincides with the onset of the rise in left ventricular pressure (Tavel et al, 1965). The upstroke is part of the pre-ejection period (PEP).

Following ventricular excitation, the trabeculae carnae and papillary muscles are first to contract. This draws the mitral valve towards the apex. The initial increase in circumference of the ventricular chamber occurs before there is any rise in intra-cavity pressure, after which the diameter, circumference and external length simultaneously expand (Rushmer, 1976). These contracting muscles elevate pressure within the ventricle but do not alter its volume.

Figure 1.2

A Duplicated Normal Apexcardiogram

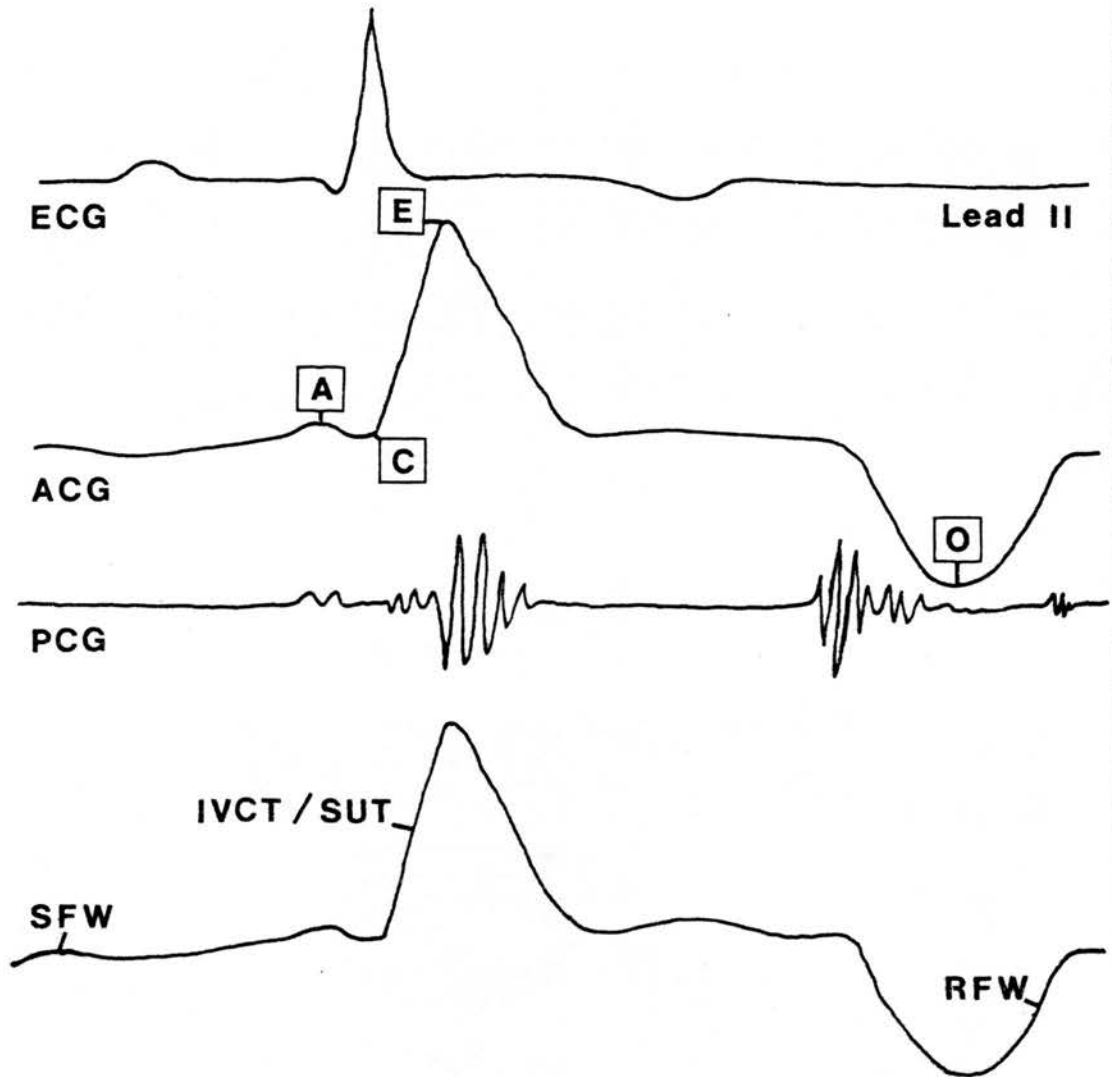
Points on the ACG : A = atrial wave; note the coincident S_4 on the PCG. C = onset of the systolic upstroke, culminating in a peak (E). O = nadir at approximately the time of opening of the mitral valve.

Intervals on the ACG : RFW = rapid filling wave SFW = slow filling wave followed, at slow heart rates, by a period of diastasis.

IVCT/SUT = isovolumic contraction time or systolic upstroke time.

Recording taken at 250 mm sec^{-1} .

Figure 1.2



This period of isovolumic contraction (IVCT) ends when ventricular pressure exceeds aortic pressure and ejection occurs (Spodick and Kumar, 1968). This should coincide with the maximal systolic peak (E point) of the ACG (Benchimol and Dimond, 1963)

During the ejection phase, ventricular emptying is rapid in early systole and later slows. This has been demonstrated as a rapid descent followed by a plateau at mid-systole (Tafur et al, 1964) descending again to the nadir or 0 point (Gibson, 1975). This is the approximate time of mitral valve opening (Legler et al, 1963).

At the beginning of the diastolic interval, all dimensions of the ventricular chamber increase rapidly. On the ACG, a brief sharp upstroke is described: the rapid filling wave (RFW). This phase merges abruptly or gradually into the phase of slow filling which persists until atrial contraction ensues. At slower heart rates, when the ventricle has plenty of time to fill, a point is reached when the ventricles are maximally extended. The slow filling phase is termed diastasis and may be indicated on the ACG as a plateau at the end of the slow filling wave (SFW). Diastole ends with atrial contraction.

1.4 Correlation of Physiologic with Abnormal Configuration

An ideal description of the cardiac movements would include both anatomic and physiologic components. It should define the structure responsible for the motion and the exact mechanism whereby it is produced (Coghlan et al, 1961). Such exactness is not always possible.

The A wave closely follows the P wave of the ECG and originates from movement of the blood into the ventricle during pre-systole. Proof that it is caused by atrial contraction is its disappearance in atrial fibrillation, its early appearance when there is prolongation of the P-R interval and its dissociation from the main ventricular wave in cases of complete heart block (Coulshed and Epstein, 1963).

If there are no P waves in the ECG, if the atrio-ventricular valves are obstructed or if the atria are incapable of contracting, there will be no A waves. Work by Craig (1971) confirms a close association between a large apical A wave and the presence of a fourth heart sound(S_4).

An exaggerated A wave is seen in left ventricular hypertrophy in man. This may be the result of aortic stenosis, systemic hypertension, acute mitral regurgitation or cardiomyopathy. The large A wave is created by a disproportionate rise in pressure with the increase in ventricular filling resulting from atrial systole. This is a manifestation of ventricular 'stiffness'. Tavel et al (1965) defined the A wave as being abnormally large if its height was 15 per cent or more of the total complex. The relationship of A to H (the total amplitude of the waveform) may be expressed as the A/H ratio.

Later work indicated that an S_4 frequently occurs despite a normal A/H ratio in subjects with severe aortic stenosis or insufficiency (Denef, De Geest and Kesteloot, 1973).

The abrupt upward movement of the ACG which is the start of ventricular contraction occurs during the isovolumic phase of systole. The onset of the rise of the ACG is precisely co-incident with the ventricular pressure curve (Craig, 1975). Therefore, it is possible to define two parts during the onset of ventricular systole: the electromechanical interval (Q-C) and the isovolumic contraction time (C-E).

The peak of the wave roughly corresponds with ejection. However, in abnormal cardiac conditions or failure, this point may not be well defined and the whole upward movement may become domed (Willemss, De Geest and Kesteloot, 1971; Sutton, Prewitt and Craige, 1970) or exaggerated (Sutton, Craige and Grizzle, 1967).

These latter (hyperdynamic) curves are of similar shape to a normal waveform but are increased in amplitude. They reflect a palpable impulse which may be noticed in mitral regurgitation and other situations where there may be a large stroke volume.

The sustained impulse is characterised by a rising plateau or dome shape (Fig 1.3). The E point (maximal systolic peak) cannot provide a marker for left ventricular dilatation (aneurysm). However, in the former condition there is a very muscular ventricle while in the latter there is a severe thinning of the muscle and yet both show the same pattern.

The diastolic portion of the wave is often exaggerated in mitral regurgitation or may be flattened in mitral stenosis.

Unfortunately, the ACG demonstrates only a limited number of patterns as a result of a large number of dissimilar and unrelated conditions. This may limit its value as a diagnostic aid.

1.5 The Concept of Myocardial Contractility

There have been many attempts to find an indicator of contractility from non-invasive measurements.

The property of contractility has interested scientists for many years. Myocardial contractility has been used widely to interpret the cardiovascular effects of drugs, exercise and heart disease on cardiac performance (Patterson, Kent and Pierce, 1972). Early studies on muscle fibre dynamics were performed on isolated preparations (Sonnenblick, 1962).

The contractile properties of isolated papillary muscle can be characterised and the contractile state defined in terms of force, velocity, length and time (Taylor et al, 1967).

Figure 1.3

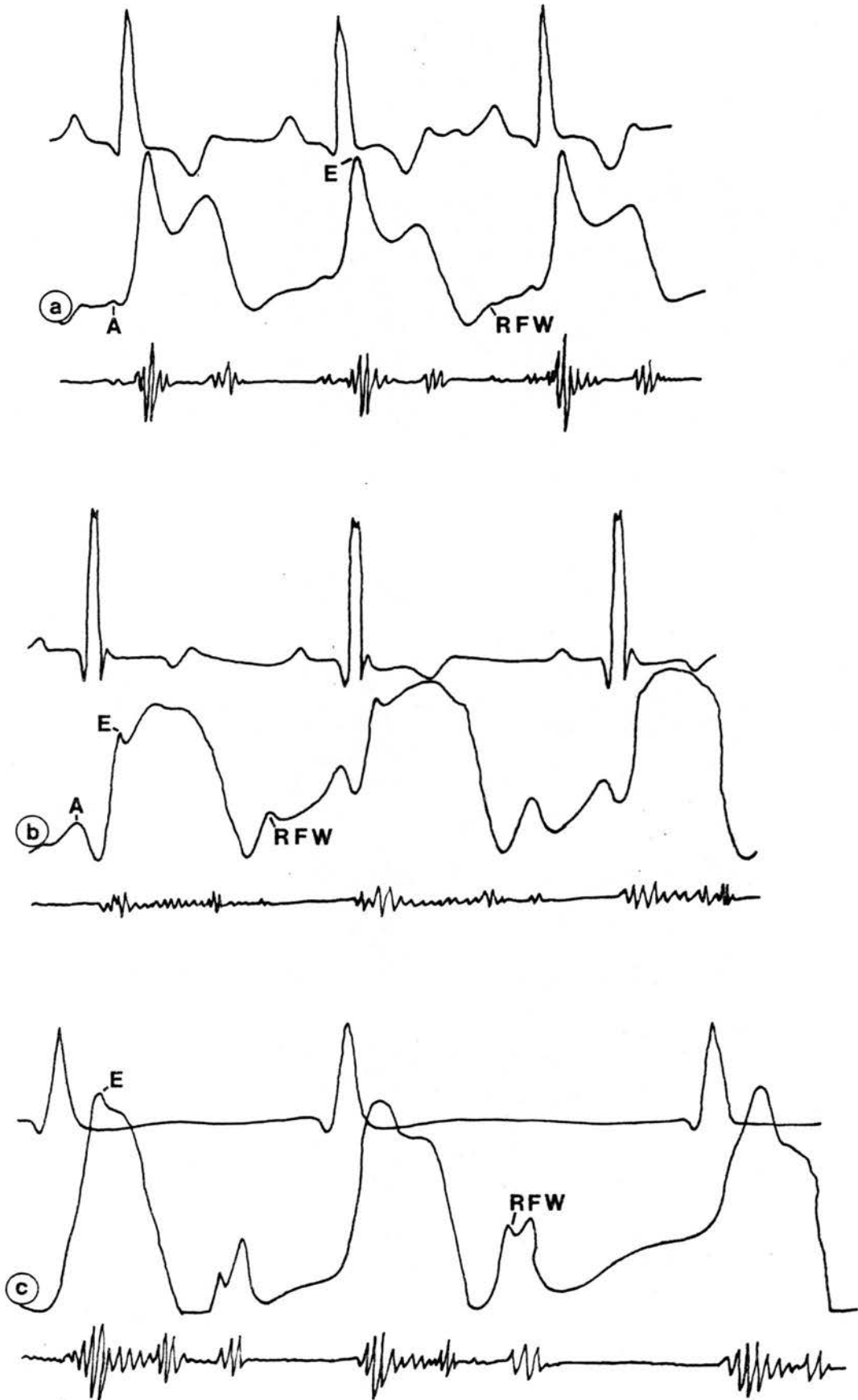
Basic Types of Apexcardiogram

Simultaneous tracings of the ECG, ACG and PCG in three dogs to demonstrate the different types of systolic curve.

- a) Normal curve : in morphology and amplitude, subject - Greyhound, female, 3 years old.
- b) Sustained curve : normal or exaggerated in height and a horizontal or rising during systole often with an exaggerated A wave. Subject - Alsation, male, $1\frac{1}{2}$ years old, with an aortic stenosis causing left ventricular failure.
- c) Hyperdynamic curve : basic morphology is the same as normal but the amplitude is grossly exaggerated. Subject - St Bernard, female, 2 years old with atrial fibrillation, severe mitral regurgitaion and gross ventricular hypertrophy.

All recordings taken at 100 mm sec^{-1} .

Figure 1.3



However, the measurement of contractile state of the left ventricle is more complicated. In vivo, contractility reflects not only the function of the heart but also the body's metabolic demands and the state of the peripheral circulation.

The definition of the term remains unclear when all the factors associated with contractility are taken into account. If heart muscle is kept at a constant length, contraction results in force generation and, according to Starling's Law, an increased muscle length results in greater force generation i.e. a stronger contraction. However if the length remains the same and a greater force is generated then this is defined as an inotropic change and may be mediated through a change biochemical, ionic or pharmacological status. (Van den Bos et al, 1973)

Changes in contractility are easy to detect if the muscle is kept at constant length. If it is allowed to shorten, then the force developed is also a function of the velocity and extent of the shortening. It is further complicated when there is a change in the time course of contraction. It may be questioned whether this is truly a change in contractility (Van den Bos et al, 1973)

The mechanical action of the heart can be influenced by acute changes in the resting fibre length (preload) and by alteration in the arterial wall force during ejection (afterload). It is generally agreed that the haemodynamic performance of the ventricle cannot provide information of the inotropic state unless these factors are constant, or at least their effects are taken into account (Ross and Peterson, 1973; Richmond et al, 1975).

The reasons for measuring the inotropic state generally fall into one of two categories: (i) assessment of a change in inotropic state after pharmacological intervention or following physiological stress; (ii) assessment of a basal level of inotropic state for the purpose of comparing one species with another, or one individual at different points in time (Ross and Peterson, 1973).

These assessments could prove very useful in both experimental and clinical work. Unfortunately, there is no simple universally applicable, valid index of contractility in the intact heart. In the search for an ideal a large number of different single indices have been proposed. Each is based on some mechanical correlate of contractile state but the estimations and assumptions which have to be made ensure that the answer is an approximation.

Henderson (1975) in a chapter on contractile state of the heart postulates that a better approach would be to study the ejection phase rather than the isovolumic period. This would avoid some of the assumptions inherent in isovolumetric analysis but would still require to be related to end-diastolic volume and load.

As the limitations of some of the established indices become clearer so they can give some useful additional information. These include maximum rate of increase in left ventricular pressure ($\max dp/dt$), time from ventricular activation to $\max dp/dt$, $\max dp/dt$ divided by a simultaneous left ventricular pressure ($\max dp/dt$ LVP) and the theoretical maximum velocity of shortening of the left ventricular contractile elements at zero-force development ($V_{ce \max}$) (Patterson et al, 1972). None are recommended without reservation (Van den Bos, 1973).

An ideal index of contractility would be easy to measure, significantly responsive to interventions known to alter contractility and it would not alter with preload changes (Patterson et al, 1972).

1.6 Quantification of Data from the ACG

In recent years the value of varying amplitude or time criteria of quantitative apexcardiography has been examined (Jezek, 1963).

Many authors have sought to correlate these parameters in the ACG with internal indices of left ventricular performance in dogs (Gay et al, 1978) and in man (Manolas et al, 1976; Venco et al, 1977).

The use of amplitude parameters in man (Voight and Friesinger, 1970) has not been entirely feasible (Denef et al, 1975; Manolas et al, 1976) because of differences among individual subjects in cardiac size and thoracic shape. Changes in ventricular volume, in firmness of the myocardium and also in the curvature of the apical region are all sensed as displacement by the recording assembly. The configuration of the systolic complex is subject to great variation depending on the spatial relationship of pick-up to apex. The amplitude of the systolic complex depends on many factors, including stroke volume but it is also affected by the thickness of the ventricle wall and the pressure applied to the transducer. For these reasons, less subjective information was sought (Rios and Massumi, 1965).

In 1951, Johnstone and Overy recognised that the magnitude of the first time derivative of the ACG was proportional to the velocity of motion of the left ventricular wall and therefore might be closely related to the functional status of the myocardium. Reale (1967) proposed using the first time derivative of the ACG in a similar way to the left ventricular dp/dt . The time interval between onset of depolarisation and peak first derivative of the ACG was measured and significant correlations with other haemodynamic and angiographic indices were found (Vetter et al, 1972).

The ACG has also been used to identify heart sounds (Benchimol et al, 1961). Auscultation of the heart is of interest to physicians because heart sounds relate directly to the chief function of the heart - its mechanical activity (Groom, 1964). Sounds heard at auscultation comprise only a small fraction of all the vibrational energy produced at the precordium.

Most of this energy is present as low frequency vibrations below the audible range. It is this part of the heart vibration spectrum which gives the displacement curves known as the ACG.

Utilised in conjunction with the ECG and ACG, the phonocardiogram (PCG) forms a permanent objective record which may be used for the purpose of timing the events of the cardiac cycle.

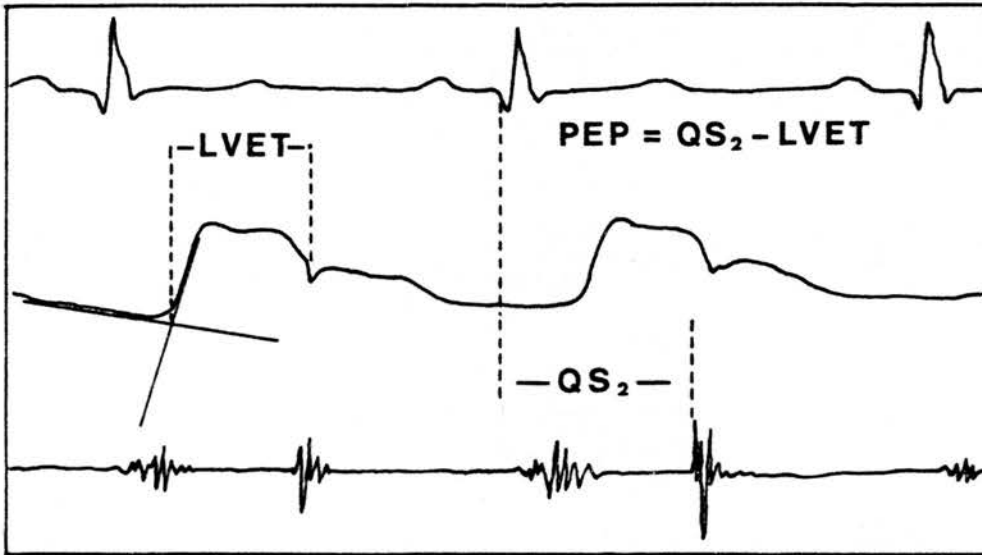
1.7 Systolic Time Intervals

The temporal phenomena of the cardiac cycle stimulated interest as early as 1874 (Garrod). It was early appreciated from work by Wiggers (1921 a & b) that the usual expressions of change in volume pressure and flow were accompanied by detectable alterations in the temporal course of the cardiac cycle. The systolic time intervals (STI) were one of the first quantitative non-invasive tests of cardiac function. Comparison with direct measurements of ventricular performance established that STI were a significant quantitative assessment.

The measurements are based principally on: total electro-mechanical systole (QS_2); left ventricular ejection time (LVET); The pre-ejection period (PEP) and the changes in ratio of PEP to LVET (PEP/LVET) (Jackson, 1974). These are unique amongst other tests of ventricular performance because time is the only variable.

STI are measured from simultaneous fast recordings of the ECG, PCG and the carotid or subclavian arterial pulsations (Lewis et al, 1974). They are derived from four temporal landmarks of the above recordings, namely: the onset of ventricular depolarisation, the upstroke and incisural notch of the carotid arterial pulse tracing and the aortic component of the heart sound (see Fig 1.4).

Figure 1.4



Systolic Time Intervals from the Carotid Arterial Pulse (CAP)

Simultaneous tracings of the ECG, CAP and PCG to show the measurement of QS_2 , LVET and the calculation of PEP. The intersection of the tangents indicates the start of the upstroke of the CAP.

(after Weissler et al, 1969; Lewis et al, 1977).

Work by Martin et al, (1971) has indicated that the use of the arterial pulse in man is invalid due to the pulse transmission delay time.

Gross et al (1974) employed carotid loops in experimental dogs to assess STI. The use of intra-arterial catheters ensures a carotid pulse but is of limited value in clinical cases owing to the effect of an invasive technique. It has been suggested that the use of echocardiography obviates the necessity for a carotid pulse or phonocardiogram (Venco et al, 1977; Pipers et al, 1978).

Studies by Kesteloot and Willems (1967), Bush et al (1970) and Manolas et al (1976) show that the ACG is a valid measurement of the onset of contraction. It has been used to further define PEP. This interval has been described as Q-C: excitation - onset of contraction (Gabor et al, 1972) and IVCT: isovolumic contraction time (Oreshkov, 1965).

1.8 Physiological Correlation with STI

There is an inverse relationship between heart rate and left ventricular ejection time in man (Lombard and Cope, 1926). Many of the interrelationships between physiological phenomena have been established in isolated heart preparations (Wiggers, 1921 a & b; Katz 1927; Frank, 1959; Wallace, et al 1963). Information derived from Lombard and Cope's study has allowed several conclusions to be drawn: an increase in heart rate causes a decrease in both QS_2 and LVET (Weissler et al, 1968 and 1969). An increase in heart rate, due to adrenergic stimulation results in reduced PEP. Increased ventricular filling causes a fall in IVCT, an increase in ejection fraction and stroke volume while QS_2 remains the same. A transient increase in afterload results in a longer IVCT, reduced ejection fraction and stroke volume while total systole remains the same or is diminished.

The situation in an intact animal is not always the same as for isolated hearts owing to the complex nature of the response to changes in blood pressure and other physiological parameters. Present evidence supports the theory that increased afterload prolongs all the systolic phases. However, a chronic increase in blood pressure has a much less striking effect on the STI, the major effect being on the PEP (Weissler et al, 1968).

Most of the above studies on STI are the result of acute interventions. Of clinical significance are the effects of sustained haemodynamic alterations associated with left ventricular disease (see Section 1.11).

PEP has been thought to represent a measure of intrinsic myocardial contractile performance (Sultan Ahmed et al, 1972). In this study, on subjects with either normal left ventricles or cardiac disease confined to the left ventricle, PEP and PEP/ LVET exhibited good correlations with measurements of pump function. The authors also claimed excellent correlations with parameters of contractility. They concluded that the contractile state is the predominant influence on the duration of the PEP. PEP is also affected to a lesser extent by activation time and preload.

These external indices have been used to follow predicted changes in contractility and to assess drug therapy and altered cardiac physiology. This assumption has been that these indices are related to the true isovolumic contraction time (Martin et al, 1971).

The inverse relationship between true isovolumic contraction time and dp/dt in the intact animal was reflected by PEP and external ICVT. The two external indices were therefore shown to reflect reliably changes in true (internal) isovolumic contraction time. The pre-ejection indices yield useful information about changes in ventricular performances including an estimate of changes in left

ventricular dp/dt . They relate directly to contractility only when diastolic pressure remains constant and left ventricular end diastolic pressure is not greatly increased (Metzger et al, 1970).

However, Lewis et al (1974) stated that the use of PEP as a measure of contractility should only be considered if all the factors affecting the left ventricle are investigated.

The PEP, like the stroke volume or ejection fraction, is a measure of overall left ventricular performance during isovolumic systole. It does not necessarily reflect the intrinsic contractile properties of the ventricular muscle.

The PEP responds in opposite fashion to negative and positive inotropic agents; the LVET is generally shortened by both. With negative inotropism the mechanism is similar to that operating in left ventricular failure. Positive inotropes increase velocity and extent of fibre shortening. The increase in velocity is the predominant effect so that LVET shortens or remains the same (Lewis et al, 1977).

1.9 The Effect of Heart Rate and Cycle Change on STI

The deviations of QS_2 , LVET and PEP have been related inversely and linearly to heart rate (Weissler et al, 1968). The normal STI corrected for heart rate provide a basis for comparison with findings in disease. The values of different phases of the cardiac cycle have been corrected according to heart rate (Benchimol et al, 1963) or it may be corrected respective to a value of 75 beats/min (Jezek, 1963).

Deviations from normal can be expressed in two ways:

(1) Calculating the predicted normal interval for the observed heart rate from the appropriate regression equation and subtracting the measured interval from this value, or

(2) Calculating the corresponding STI index: QS_2I , $LVETI$, $PEPI$. These are obtained by transposition of the terms in the regression equation and calculated as the sum of the measured interval and the product of the observed heart rate and the appropriate normal regression slope. This facilitates comparisons between subjects (Lewis et al, 1974).

In the heart rate range 40-110 beats/min the durations of QS_2 , $LVET$ and PEP are linearly related to heart rate (Weissler et al, 1968 and 1969). Normal subjects in the basal state exhibit a narrow range of time intervals relative to heart rate. The isovolumic contraction time ($IVCT$) remains constant over a wide range of heart rates. The inverse relationship between the duration of electromechanical systole and heart rate is due primarily to the shortening of left ventricular ejection.

Heart rate in dogs may vary greatly depending on breed. There may also be beat to beat changes resulting from respiration. Wallace et al, (1963) described the effect of different determinants on the duration of phases of systole in dogs. A healthy resting dog has a heart rate of 45-120 beats/min. An increased rate altered the durations of the phases of systole directly. Changes in velocity and acceleration of flow influenced the cycle length.

Evidence from Muir and Hamlin (1973) suggested that ventilation per se had very little effect on the systolic duration in dogs. Measurements taken during expiration allowed the heart rate to stabilise and cycle to cycle changes became very small. The R-R' interval varied less than 4mm between beats in another study (Weissler, 1972).

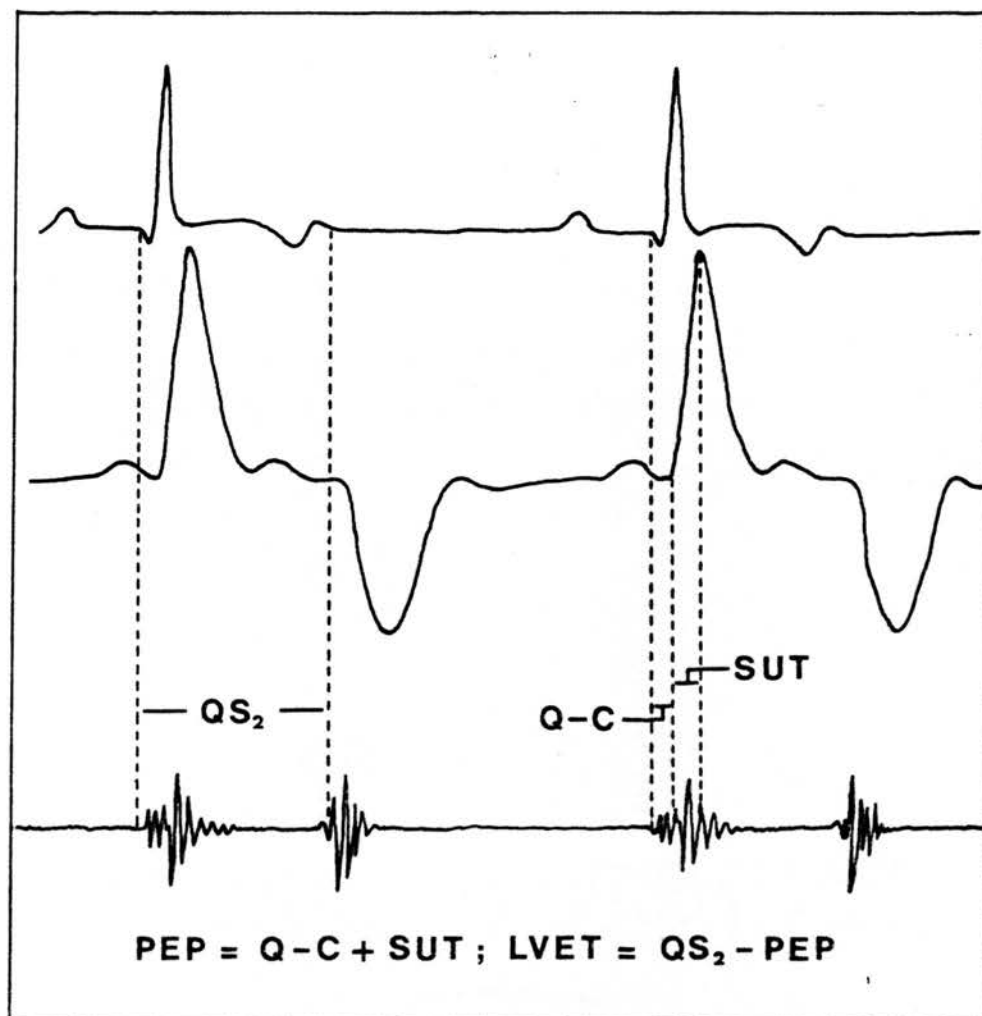
1.10 Use of the Apexcardiogram to obtain STI

The ECG and PCG are easily obtained in the dog but the carotid artery lies deep in the neck and its pulsations are not transmitted to the surface with sufficient strength to produce an accurate pressure pulse. One alternative is to use the ACG as reported in Gay et al's paper (1978).

The ACG reflects ventricular pressure changes and is similar to the LV pressure curve. The upstroke and nadir of the ACG in dogs was found to be markedly similar to the LV pressure at rest and during variations of preload, afterload, HR and inotropic state (Willems, Kesteloot and De Geest, 1972). These observations confirmed the value of the ACG for timing intracardiac events (Craigie, 1975) (see Fig 1.5).

Some studies in humans have recorded the ACG with a concurrent carotid pulse tracing. Other workers have used just the ACG (Benchimol et al, 1961; Benchimol and Dimond, 1963).

The ACG is an excellent method for recording the onset of movements in systole - for instance the onset of IVCT (Oreshkov, 1965). In this respect, the ACG has the significance of being a direct method of recording. While the rise of ventricular pressure appears as a result of the muscular contraction, it does not directly reflect the mechanical activity of the heart and shows some lag in comparison with the ACG.



Definition of Systolic Time Intervals from the Apexcardiogram:

Simultaneous recordings of the ECG, ACG and PCG in a normal Beagle.

QS_2 = total electromechanical systole

$Q-C$ = electromechanical interval

SUT = systolic upstroke time

$LVET$ = left ventricular ejection time

Recordings taken at 100 mm sec^{-1}

The IVCT starts when the A-V valves shut - they close when ventricular pressure exceeds atrial pressure. The C point of the ACG demonstrates this clearly in a good tracing (Lewis et al, 1974; Bush et al, 1970; Waagstein et al, 1974). This allows the PEP to be defined as two intervals: Q-C (electromechanical delay - EMD) and the IVCT or systole upstroke time (SUT). It has been postulated that the EMD may be prolonged in heart disease (Oreshkov, 1965). The SUT has been measured as an interval (Manolas et al, 1976). Assessment of the rate of rise of the slope (dA/dt) has been considered in attempts to measure contractility (Reale, 1967). Significant correlations have been discovered between the peak derivative of both the ACG and LV pressure (Denef, De Geest and Kesteloot, 1973).

The ejection sound of the PCG has been used to indicate the end of the IVCT. This is often unidentifiable in practice. The E point of the ACG has been considered as occurring at the start of ejection (Benchimol and Dimond, 1963; Tafur, Cohen and Levine, 1964). Other workers noted that the E point is not always a true representation of ejection (Tavel et al, 1965) especially in traces which the E point is slurred and in patients with abnormal contraction patterns (Sutton et al, 1970). The real E point may be found towards the end of the upstroke as a notch and this is not always easily perceived. The peak of the ACG should precede the start of the upstroke of the carotid pulse by the delay period of the pulse transmission time. This is very often the case in sharp peaked ACGs which tends to indicate that the E point approximates to the start of ejection.

There is no absolute physiological landmark for the end of systole which can be derived externally. The QS_2 interval ends with the initial high frequency vibrations of the aortic component of the second sound (S_2). It represents an estimate in which easily identified physiologic landmarks are employed (Lewis et al, 1977). Studies by Luisada et al (1978) demonstrate that the incisural notch and the initial high frequency vibrations of the S_2 nearly coincide and follow aortic valve coaption by less than 5msec in man.

The duration of systole (QS_2) is one of the remarkable constants of the circulatory system. Most types of heart disease may produce profound alterations in cardiac performance, manifest by directionally opposite changes in PEP and LVET but usually the QS_2 remains unchanged. When calculated with respect to HR, QS_2 will usually only be influenced by drugs.

1.11 Clinical Application of STI

The verification that external time measurements were accurate and their correlation with other parameters of cardiac function (Martin et al, 1971) allow the diagnostic and prognostic use of STI in medicine. They provide a quantitative estimate of the effect of various cardiovascular diseases of the left ventricle (Lewis et al, 1977). The timing of intracardiac events can only take place if the landmarks on the trace are not obliterated, as for instance occurs in severe left ventricular hypertrophy. It has been estimated that in humans, ACGs cannot be recorded in some 15 per cent of individuals (Craige, 1975).

In normal subjects the STI vary inversely and linearly with heart rate. The relationship may be described by a regression equation which provides a basis for study of the alterations induced by heart disease (Weissler et al, 1969). However, the presence of valvular disease, drugs and certain dysrhythmic conditions may alter these relationships and should be considered during STI interpretation (Lewis et al, 1974). Left ventricular dysfunction produces lengthening of the PEP and shortening of LVET with little change in QS_2 . Deviations in the PEP and LVET have been significantly correlated with the stroke volume and cardiac output (Weissler et al, 1969; Lewis et al, 1974) and the ejection fraction (Garrard et al, 1970).

From this information it is known that left ventricular failure lengthens the PEP and decreases the LVET (Sultan Ahmed et al, 1972). This increase in PEP is attributed primarily to a diminished rate of rise of left ventricular pressure (Lewis et al, 1974). This is related to an ineffective rate of force generated by the left ventricle during systole. The time required for the intraventricular pressure to reach arterial diastolic pressure levels is lengthened (Weissler et al, 1969). In chronic left ventricular disease with diastolic stiffness, the PEP may also be prolonged if preload is inadequate.

LVET shortening is a more complex result of heart failure. One factor affecting it is the concurrent lengthening of PEP which causes a delayed onset of ejection. In the failing heart, the velocity of fibre shortening is reduced, which logically should produce a prolonged LVET. However, the extent of fibre shortening is also reduced and this tends to shorten the LVET. This effect apparently predominates (Lewis et al, 1977).

The absolute size of the stroke volume does not determine LVET: the end diastolic pressure plays a part in altering the ejection time. Diminished preload reduces stroke volume and shortens LVET (Lewis et al, 1977).

The diagnostic value of the STI for left ventricular dysfunction can be enhanced by determination of the ratio of PEP to LVET. The deviations from normal in PEP and LVET have been identified in patients with heart failure. Since the PEP lengthened and the LVET was reduced but QS_2 remained unchanged, the ratio of the two intervals encompassed a single expression of the changes in heart failure. The PEP/LVET tended to remain within narrow limits among normal subjects even when uncorrected for heart rate and sex (Weissler et al, 1969).

The PEP/LVET may identify LV dysfunction when either (or both) the PEP and LVET indices are still within the normal range (Lewis et al, 1977). The ratio has been found to be increased in patients with heart disease (Sultan Ahmed et al, 1972). Sustained diastolic hypertension tends to increase the PEP and PEP/LVET slightly in heart failure (Weissler et al, 1968).

The ratio appears to show deviations from normal when the cardiac and stroke indices are within normal limits which suggest it is a more sensitive index of cardiac function. Many patients with left ventricular dysfunction maintain a normal cardiac index by compensatory tachycardia. If there is an increased end-diastolic volume, the stroke volume may be normal with a less than normal extent of fibre shortening (Lewis et al, 1970). In human medicine, the STI have been studied in clinical cardiac disease.

1.11.1 Myocardial Disease

The STI, as parameters of cardiac pump function (Sultan Ahmed et al, 1972), may also be useful parameters of cardiac muscle function which relates to the contractile state of the left ventricular myocardium (Metzger et al, 1970; Tally, Meyer and McNay, 1971; Aronow, Kaplan and Ellistad, 1969). Myocardial disease, in the absence of valvular regurgitation, causes a delay in onset of left ventricular ejection (Jezek, 1963) which results in a prolonged PEP, shortened LVET and an increase in the PEP/LVET ratio (Garrard, Weissler and Dodge, 1970). Increased PEP and PEP/LVET relate to depressed ejection fraction and reduced left ventricular dp/dt (Gibson, 1975). If the heart rate and QS_2 is constant, then clearcut changes in PEP and PEP/LVET may indicate that the contractile state is changing (Ahmed et al, 1972).

Whitsett and Naughton (1971) noted that the PEP was longer in patients with chronic ischaemia of the myocardium but the STI may not be sensitive enough to predict haemodynamic abnormalities that are not clinically obvious (McConahay, Martin and Cheitlin, 1972)

In acute myocardial infarction a characteristic abnormality is the reduction in QS_2 interval (Jezek, 1963; Lewis et al, 1972; Martin, Shaver and Leonard, 1972) the maximum alteration from normal at five days. This correlates very closely with the increase in catecholamine excretion (Lewis et al, 1972). PEP may be normal or prolonged, LVET shortened and the PEP/LVET not significantly different from normal (Gibson, 1975). The importance of serial STI measurements is stressed by several authors.

1.11.2 Valvular Disease

The STI appear most useful in the evaluation of patients with myocardial disease (Lewis et al, 1974). The time intervals in mitral regurgitation are less well understood than in other valve lesions.

The STI are often normal and despite the large left ventricular stroke volume, a prolonged LVET is unusual (Garrard, Weissler and Dodge, 1970). This may be due to regurgitation of blood into the left atrium prior to the opening of the aortic valve. Mitral valve disease is often accompanied by intrinsic left ventricular disease in humans (Sutton, Craige and Grizzle, 1967) and sometimes in dogs and it may be this dysfunction which gives rise to abnormal STI. If hypertension is a feature of the disease, only if there is left ventricular failure will the STI deviate from normal. (Weissler, Harris and Schoenfeld, 1968).

1.11.3 Aortic Stenosis

Despite the stroke volume being normal or decreased, severe aortic stenosis may be accompanied by an increase in LVET (Benchimol, Dimond and Shen, 1960). The PEP is usually shortened which results in a PEP/LVET lower than normal. If the patient goes into failure, then the LVET shortens as PEP lengthens, as described in Section 1.8. Following treatment and reversal of decompensation, the abnormal STI may "reappear" (Lewis et al, 1974).

1.11.4 Pericardial Disease

In the presence of pericardial tamponade there may be marked respiratory variations in LVET. These should be differentiated from the respiratory variations obtained in some patients with chronic heart and lung disease, (Lewis et al, 1974). In normal dogs, ventilation has little effect on either PEP or LVET (Muir and Hamlin, 1973) so any marked deviation in STI from normal relating to respiration may indicate some abnormality.

1.11.5 Conduction Defects

Left bundle branch block results in PEP prolongation. LVET may not alter. It is unclear which sub-interval of PEP is affected. (Adolph, Fowler and Tanaka, 1969). Lewis et al, (1974) suggest the use of the ACG to define which interval (electromechanical delay or the IVCT) is abnormal.

1.11.6 Dysrhythmias

Atrial fibrillation: in this condition the LVET is directly related to the duration of the preceding R-R interval. At longer R-R intervals the LVET lengthens rather less than expected. The relationship is non-linear unless cycle length is expressed as $60/R-R$ of the previous beat (Schoenfeld et al 1963). The PEP also relates to $60/R-R$ of the previous beat but it lengthens rather than shortens with shorter R-R intervals (Sherman and Lewis, 1972). Lewis et al (1974) postulate that this unexpected increase in PEP at faster heart rates may be related to two factors: the greater isovolumic pressure which has to be developed and a diminished preload. Since PEP increases and LVET decreases, the PEP/LVET increases with shortening cycle length. For other dysrhythmias, few studies are available for reference. Premature ventricular contractions result in a prolonged PEP and shortened LVET. The post-extrasystolic beat has a shorter PEP and a longer LVET than normal beats, which is probably due to the enhanced diastolic filling. The major drawback in STI measurement in tachydysrhythmias is the rapid heart rate and the fact that adequate preload cannot be assumed (Lewis et al, 1974).

Weissler (1972) states that to use STI in clinical situations, it should be realised that they provide cardiac performance data unlike other haemodynamic information.

The relevant factor is that these non-invasive measurements deviate from normal at the same time and in parallel with other haemodynamic measures. Perfect correlation with other variables should not be expected since they encompass different events, i.e. time rather than pressure or volume.

1.12 Aims of this Study

The work described in this thesis was undertaken to find a satisfactory method of assessing cardiac function in the dog. The main criteria were that the techniques used should be:

- (i) non-invasive
- (ii) quickly and easily accomplished
- (iii) repeatable often as desired
- (iv) suitable for use in dogs with heart disease
- (v) inexpensive in initial equipment costs

SECTION TWO

EARLY EXPLORATIVE WORK

2.1 Introduction

The movements at the precordium are produced by several factors reflecting changes in the volume of the heart, and to a lesser extent, the pulsation of the great vessels. Most observers would agree that it is the motion of the left ventricle which causes the low frequency deflections which can be recorded on the apexcardiogram (Coulshed and Epstein, 1963). Before the ACG could become a reliable indication of cardiac function these vibrations had to be correlated with the hemodynamic events within the left ventricle. The movements of the cardiac apex are not random; they can be consistently recorded and represent the consecutive phases of the cardiac cycle (Tafur, Cohen and Levine, 1964). Studies by several groups defined the points of the ACG with reference to the electrical, acoustic and mechanical activity of the heart in man and dogs (Benchimol and Dimond, 1963; Tafur, Cohen and Levine, 1964; Tavel et al, 1965).

Dogs have been used as the experimental model in many studies (Benchimol and Dimond, 1963; Willems, De Geest and Kesteloot, 1971; Willems, Kesteloot and De Geest, 1972; Deneff, De Geest and Kesteloot, 1973). But few studies have been done on dogs in their own right (Gay et al, 1978). In this section, an assessment was made of variations in ACGs from different areas of the precordium. Familiarity with the technique then ensured recordings of sufficient quality for analysis.

2.2 Materials and Methods

2.2.1 Experimental Preparation

Apexcardiograms were recorded in five Beagle type dogs (3 male and 2 female) with a weight range of 8.5 - 21.0 kgs. The dogs were fasted for twenty four hours prior to the administration of anaesthetic. On admittance to the laboratory each animal received a thorough health check. The anaesthetic procedure is fully discussed in Section 3.2.1. Once the dog was unconscious the thorax was shaved in a band encircling the rig cage, starting behind the fore limb and extending caudally for 220 mm (Fig 2.1).

2.2.2 Recording Equipment

All measurements were recorded on an eight - channel, ink jet Mingograf 82 (Siemens-Elema) which has a fast response and excellent linearity (see Appendix 1). A Siemens EKG - amplifier, type 850 was used to record lead II which gave a good definition to the Q wave. The PCG was recorded with a Siemens Phono - amplifier, type 858. The frequency bands selected were either 50 or 100 Hz. The sensitivity level chosen varied between dogs. The ACG was obtained through a Siemens Pulse Amplifier, type 859, which allowed the use of the long time constant (3 or 7 secs), necessary for pulse wave recording. A Siemens Pulse Phono Transducer allowed the simultaneous pick up of heart sounds and apical pulse wave. This is an air-coupled crystal microphone using a single piezo-electric crystal. The signal from the ACG was fed through a Siemens contractility calculator, type 868, in order to obtain the max dA/dt .

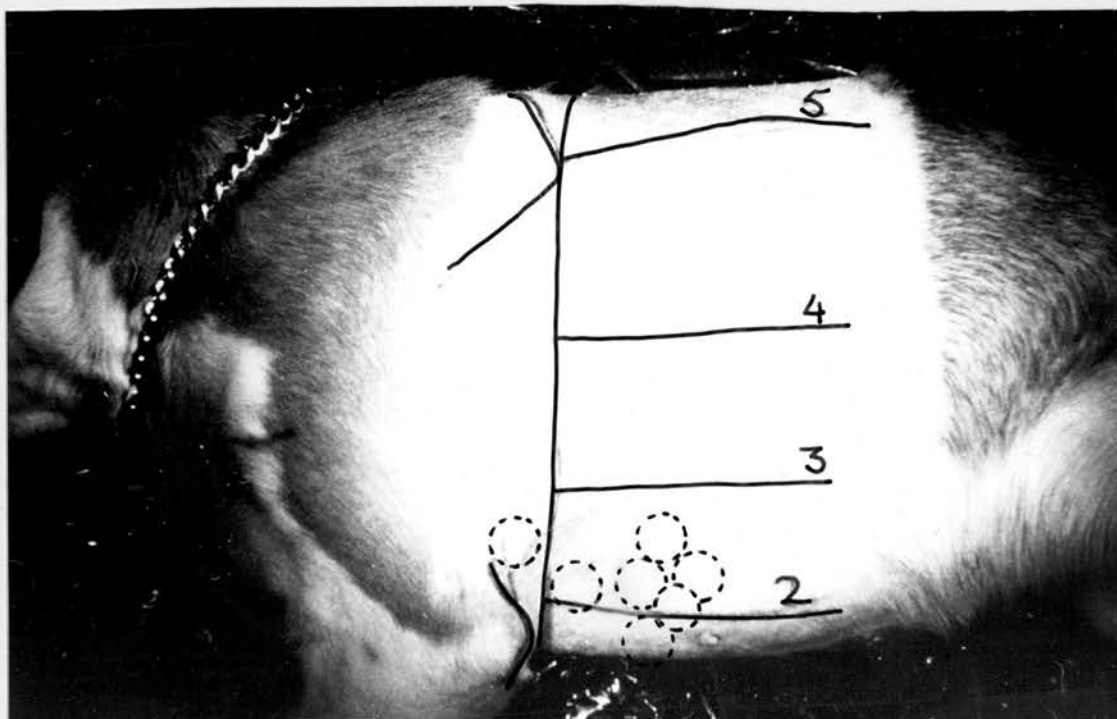


Illustration of a beagle, anaesthetised and prepared for apexcardiogram recording.

2.2.3 Recording Technique

The standard ECG limb leads were attached to the dog by hypodermic needles placed subcutaneously. The animal was laid in lateral recumbency on a foam - covered table. The transducer, held with two fingers and a thumb was placed against the thorax. A wide area around the point of maximal pulsation (determined by palpation) was explored and recordings of simultaneous ECG, PCG and ACG taken. The transducer was placed both over the ribs and in the intercostal spaces, care being taken to maintain steady pressure and to maintain an airtight seal between the rim of the transducer and the surface of the chest. In some positions, the angulation of the transducer was varied and where the waveform demonstrated a difference in either amplitude or shape, a separate recording was taken. Recordings from any one position were made over at least two respiratory cycles and were taken from the uppermost side followed by the underside. The dog was then turned over and the process repeated. The natural landmarks of the forelimb were used in conjunction with the ribs and intercostal spaces to permit precise recording of the site of the transducer (Fig 2.2).

The reproducibility of the ACG was assessed in each dog, a recording being taken one month apart on three occasions.

Figure 2.2

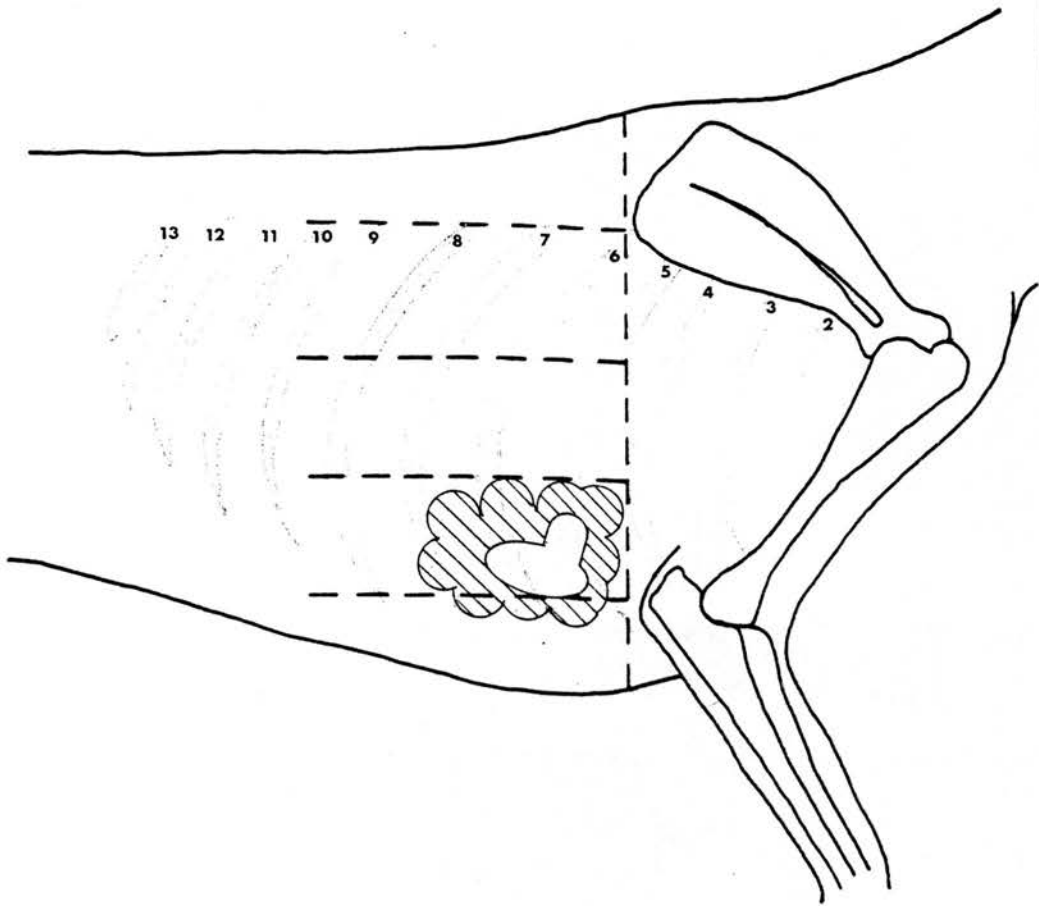
Schematic Diagrams of a Dog's Thorax

To show the area(s) of maximal apical impulse within the region over which recordings were taken (shaded).

The ribs are shown marked 2-13 and the grid refers to the natural landmarks of the forelimb:

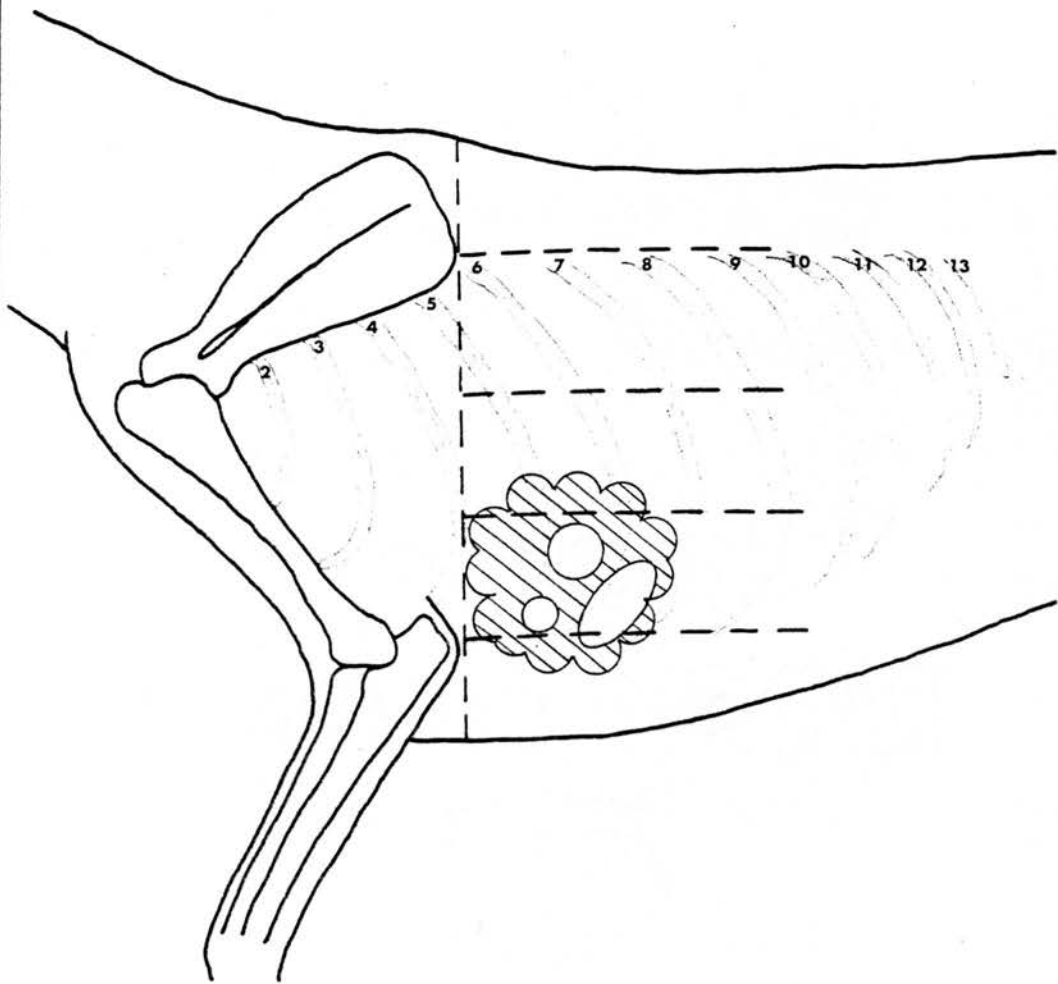
- (i) caudal angle of scapula
- (ii) point of shoulder
- (iii) mid-humerus
- (iv) point of elbow
- (v) vertical line joining (i) and (iv)

Figure 2.2 (a)



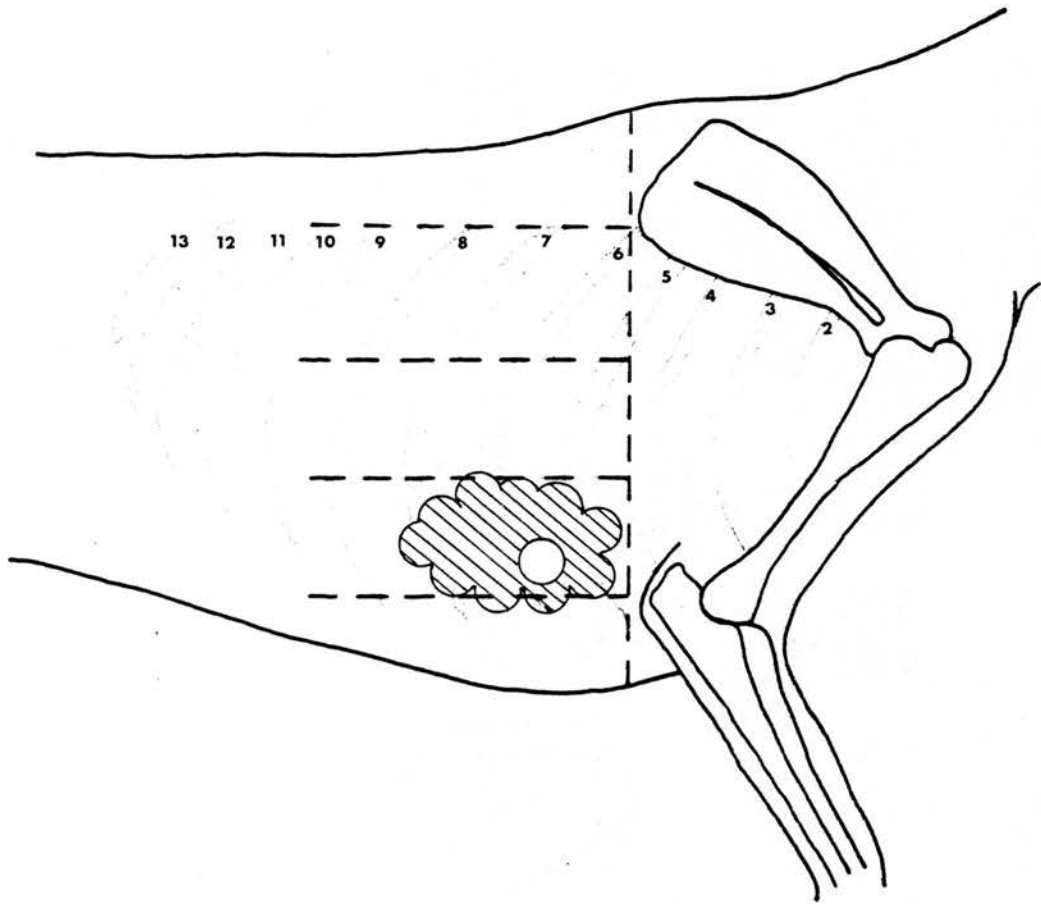
Right Lateral recumbency, recording from right side.

Figure 2.2 (b)



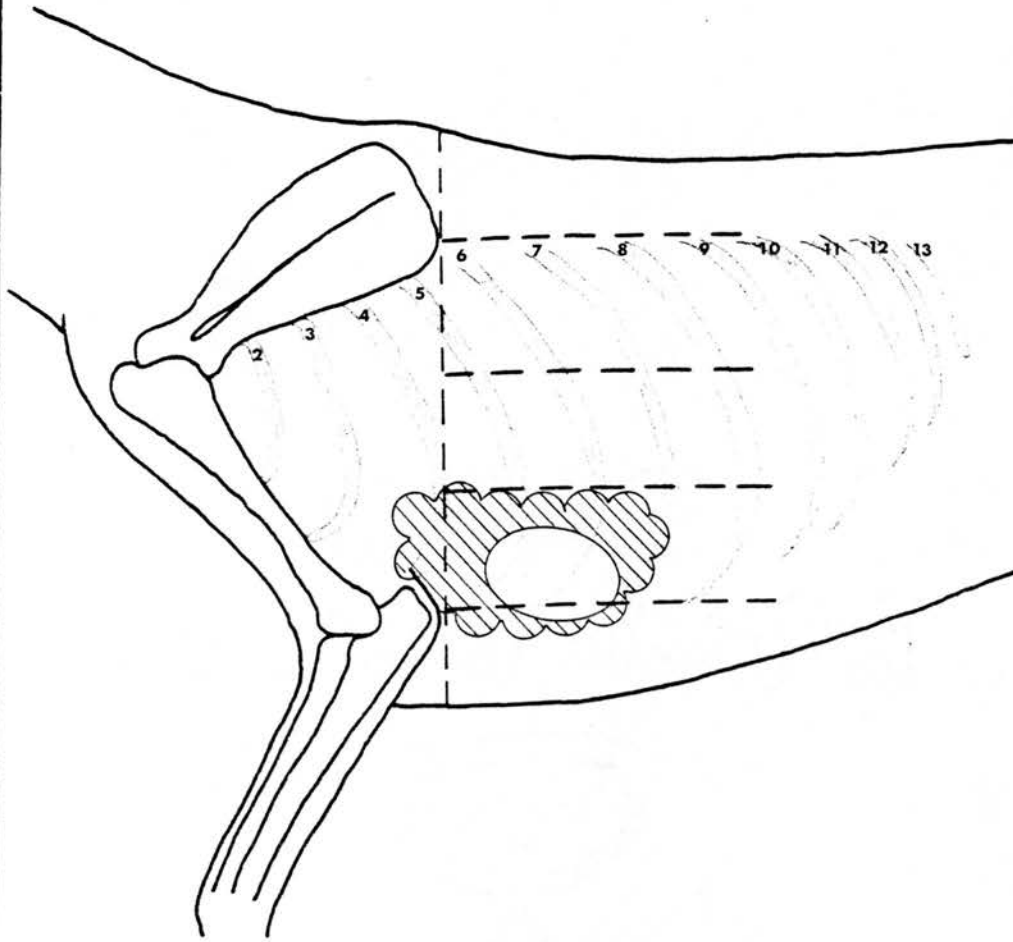
Right lateral recumbency, recording from left side.

Figure 2.2 (c)



Left lateral recumbency, recording from right side.

Figure 2.2 (d)



Left lateral recumbency, recording from left side.

2.3 Results

The apex beat was clearly visible on the left thorax except in those dogs with a broad chest, heavy loose skin or in moderately to very obese animals. The apical impulse could be palpated in all the experimental dogs examined, although during later work (Section Four) it was quite often found to be difficult or impossible to feel the movement. The area of maximum visibility/palpation was explored, followed by the perimeter around this area until no waveform could be obtained.

In all five dogs the area of exploration was nearly identical. The apex beat was visible on the left hand side of the thorax between ribs 5 & 7 in all the dogs except one. (see Table 2.1) The results from dog no.3 are illustrated in Fig. 2.3 - 2.6 and resemble quite closely the pattern obtained from the other dogs.

To demonstrate the variety of waveforms, tracings from one dog, no.3, are presented. The other dogs in the group gave a similar range of recordings. The strongest impulses were obtained on the left side of the thorax (Fig. 2.5) and the amplitude was further enhanced if the animal was lying on this side (Figs. 2.6 a & b). A right heart cardiogram was also obtained but the waveform tended to be of low amplitude and the shape was very inconsistent. (Figs. 2.3 & 2.4).

Waveforms could be obtained if the transducer was held over a rib but the amplitude was attenuated and the waveform became unstable at inspiration (Figs. 2.7 a & b). A small change in angulation without altering position could result in an acceptable waveform becoming meaningless. (Fig.2.8).

Fig 2.9 shows recordings from dog No.2 taken from the same sites with an eight week interval. The waveforms very closely resemble each other.

TABLE 2.1 DETAILS OF DOGS

<u>APEX BEAT VISIBLE/PALPABLE</u>							
<u>DOG</u>	<u>SEX</u>	<u>WEIGHT</u>	<u>LLR</u>		<u>RLR</u>		<u>EASE OF RECORDING</u> <u>1(DIFFICULT) - 5(EASY)</u>
			<u>LHS</u>	<u>RHS</u>	<u>LHS</u>	<u>RHS</u>	
1	Female	8.5 kgs	V/P	V/P	V/P	P	4
2	Female	15.4 kgs	V/P	V/P	V/P	P	3
3	Male	16.1 kgs	V/P	V/P	V/P	-	5
4	Male	18.1 kgs	V/P	V/P	V/P	-	3
5	Male	21.0 kgs	P	-	P	-	2

V = Visible

P = Palpable

LLR = Left Lateral Recumbency

RLR = Right Lateral Recumbency

LHS = Left side of thorax

RHS = Right side of thorax

Figures 2.3 - 2.6

Dog Number 3

Variations in Apex Waveforms

From different areas of the thorax.

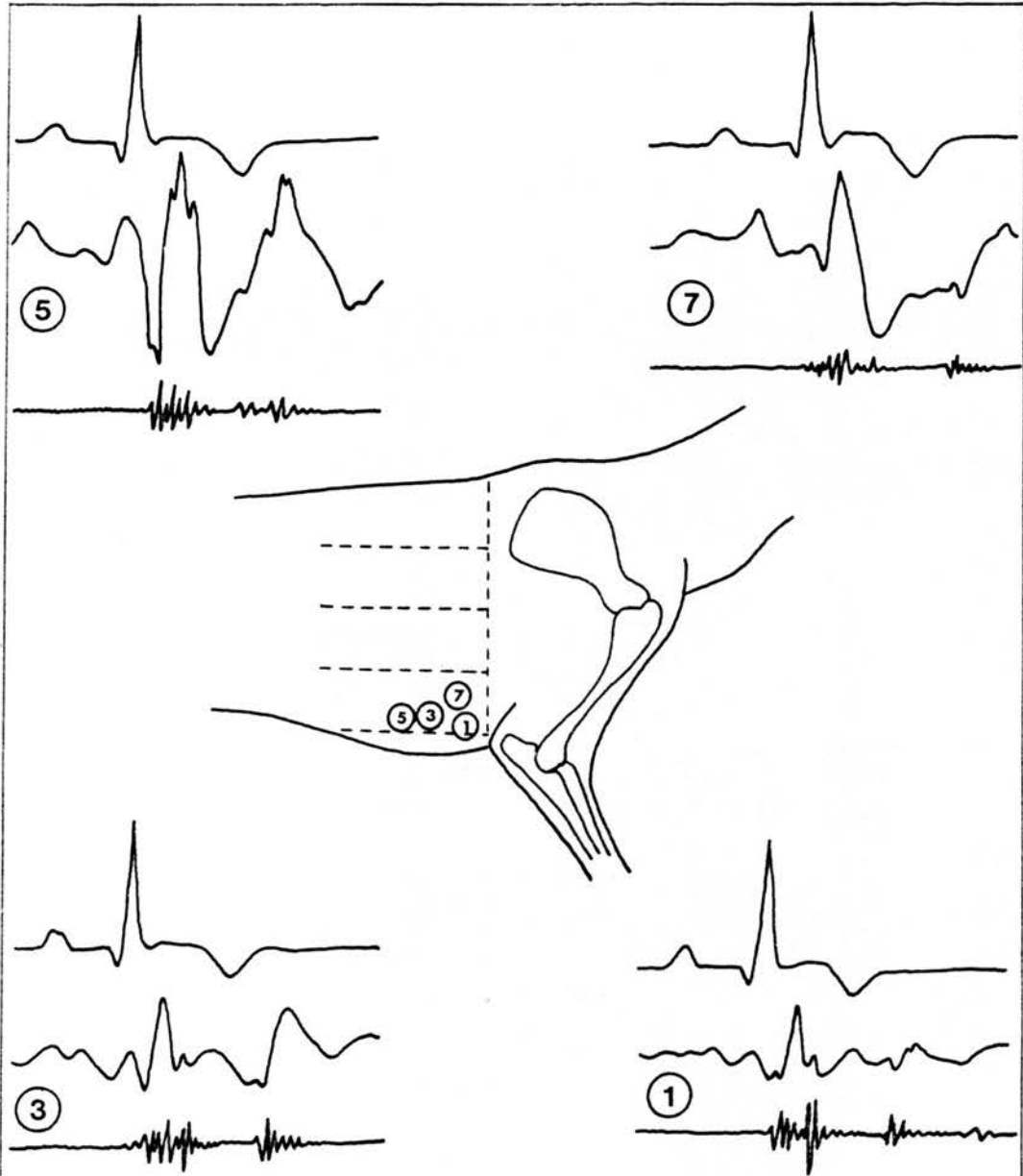


Figure 2.3

Right lateral recumbency, recordings from the right side.

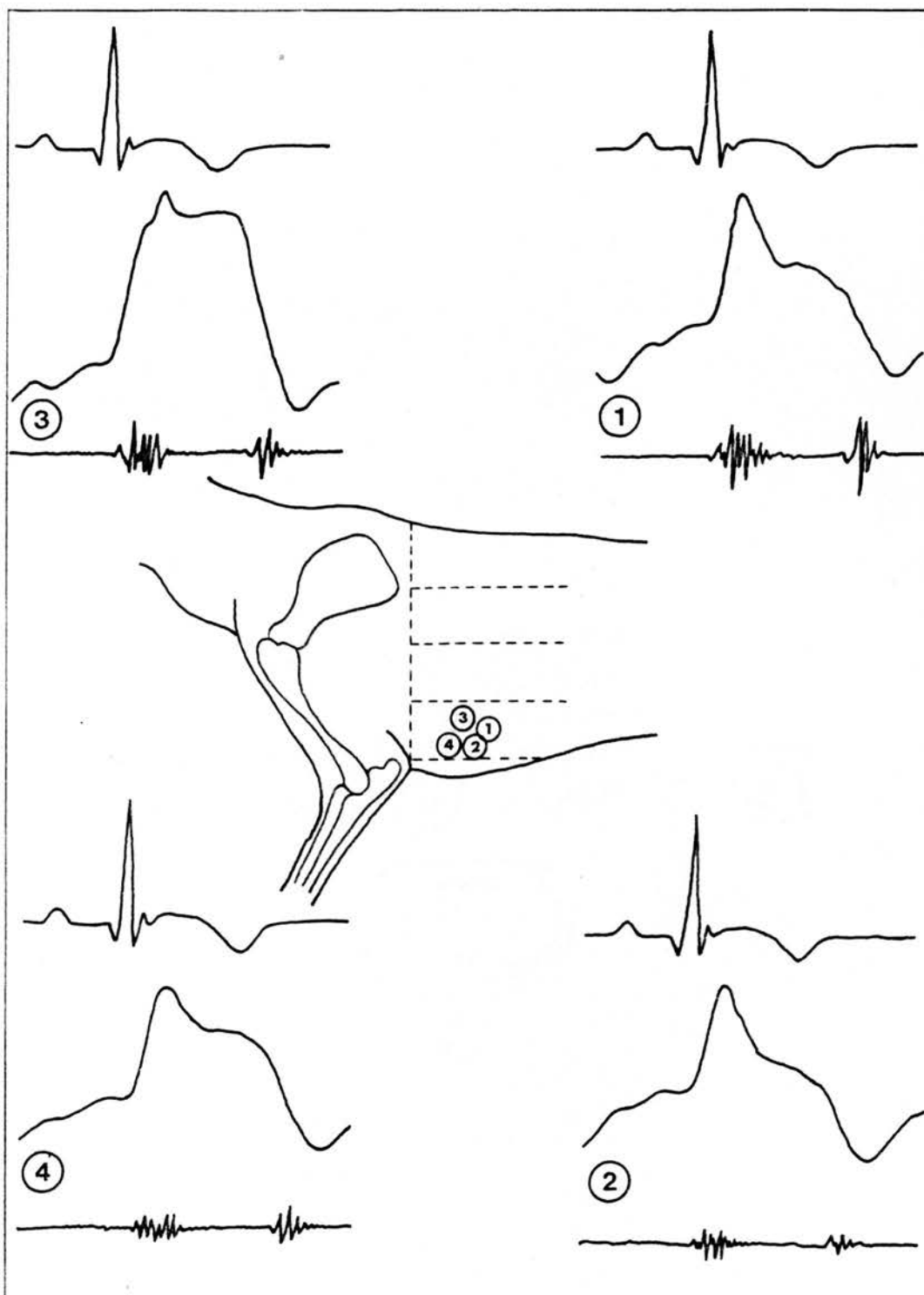


Figure 2.4

Right lateral recumbency, recordings from the left side.

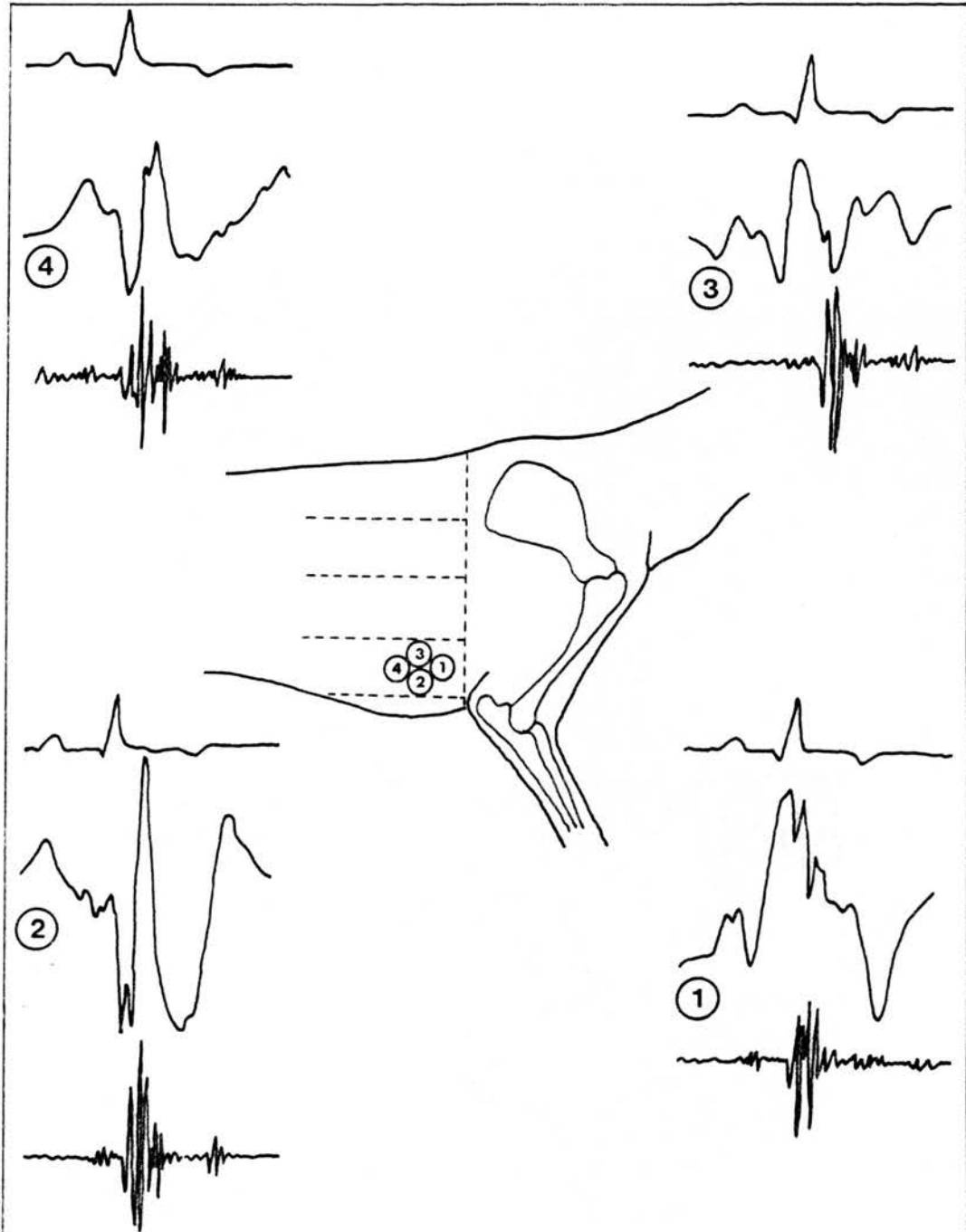


Figure 2.5

Left lateral recumbency, recordings from the right side.

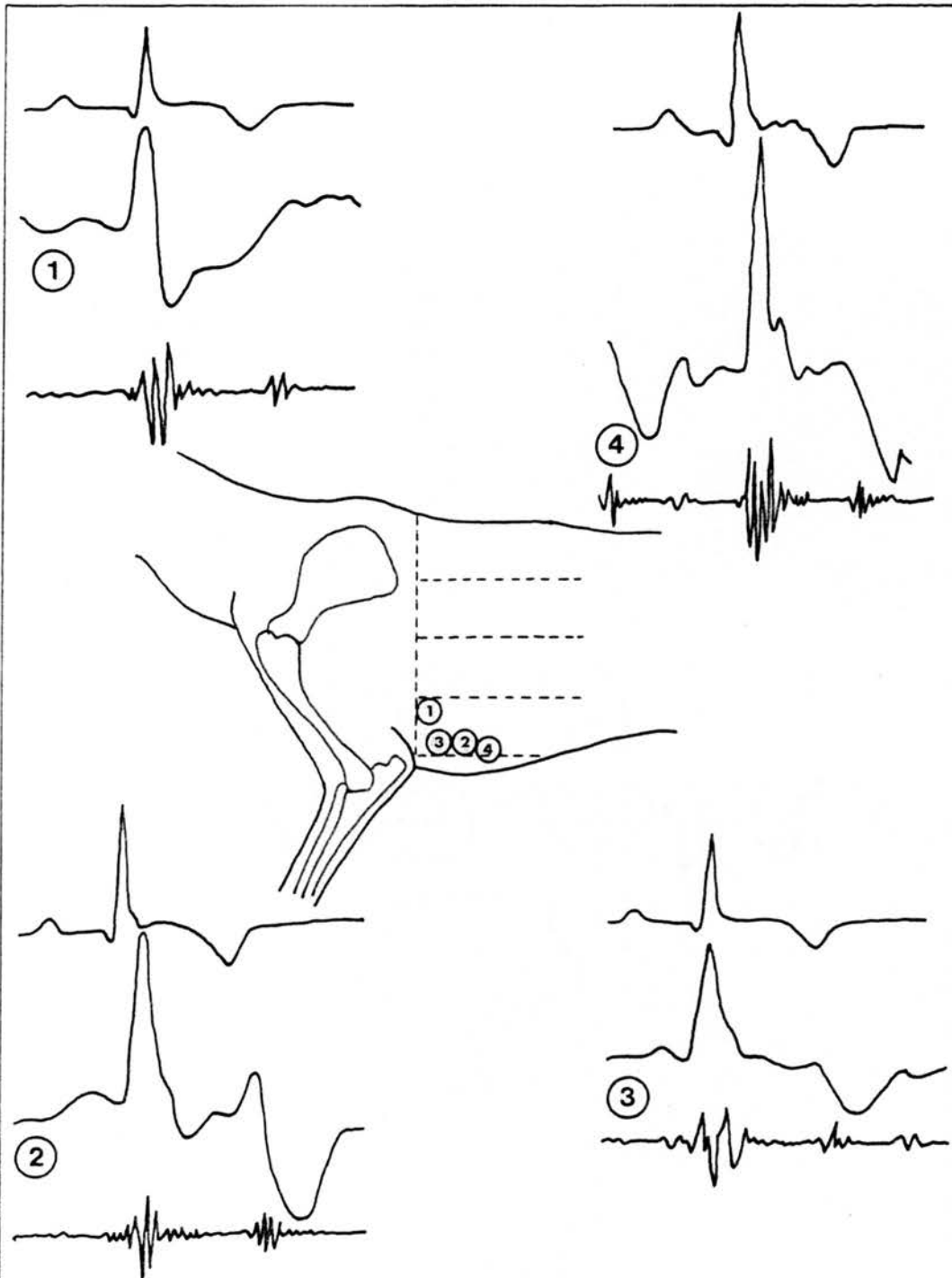


Figure 2.6 (a)

Left lateral recumbency, recordings from the left side.

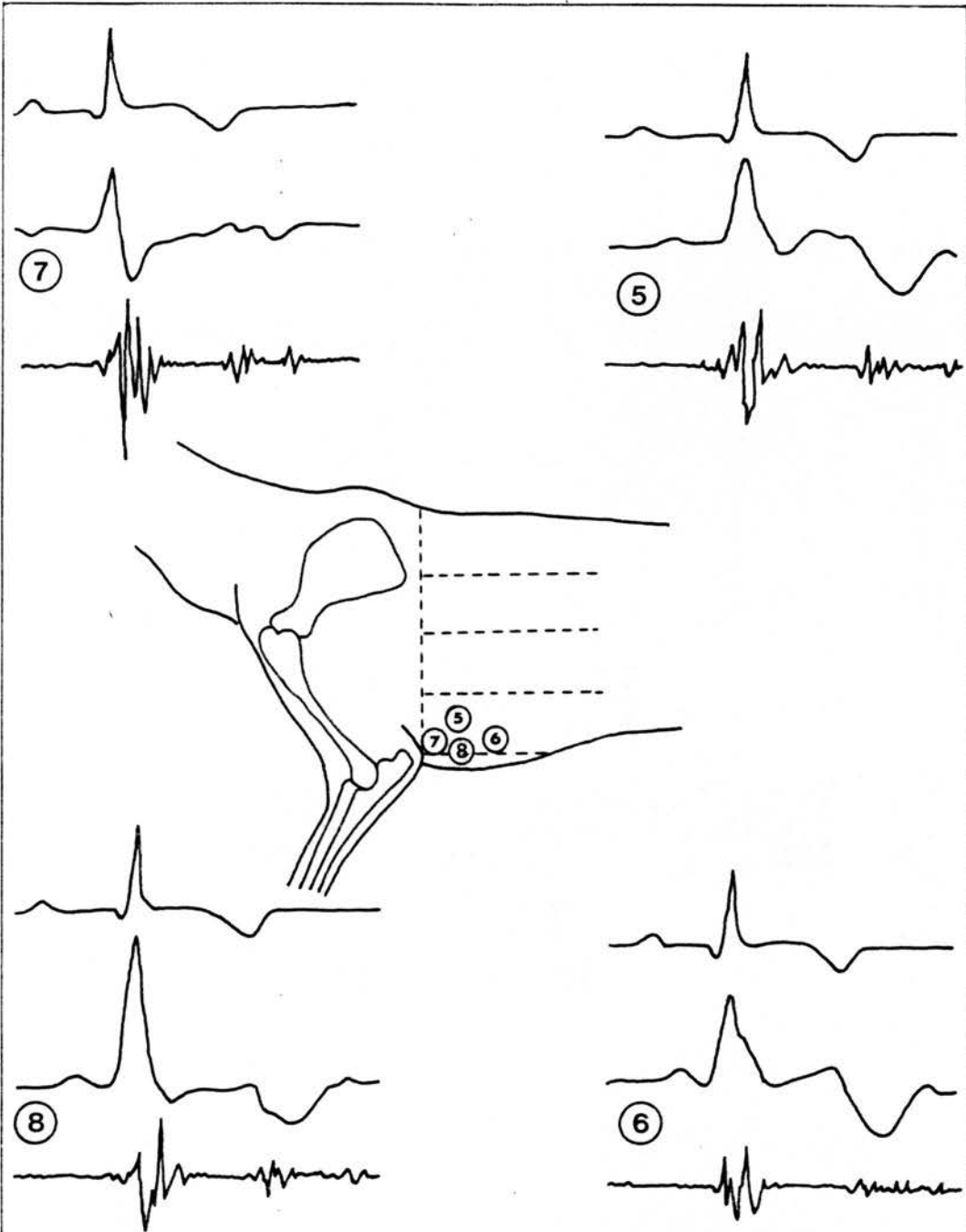


Figure 2.6 (b)

Left lateral recumbency recordings from the left side (cont'd)

Figure 2.7 (a) & (b)

Distortion of the Apexcardiogram during Respiration

Inspiration (Insp) and expiration (Exp) are marked on the traces of simultaneous ECG, ACG and PCG.

(a) Dog No.1

(b) Dog No.2



Figure 2.7 (a)

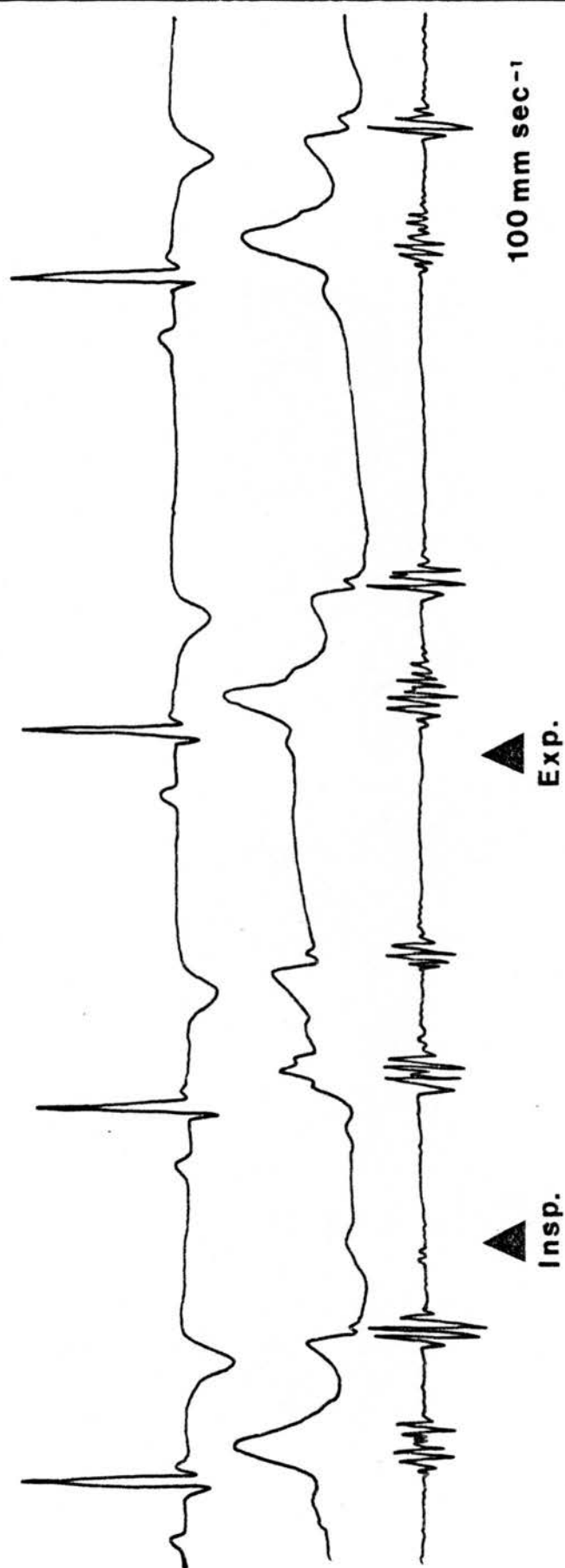


Figure 2.7 (b)

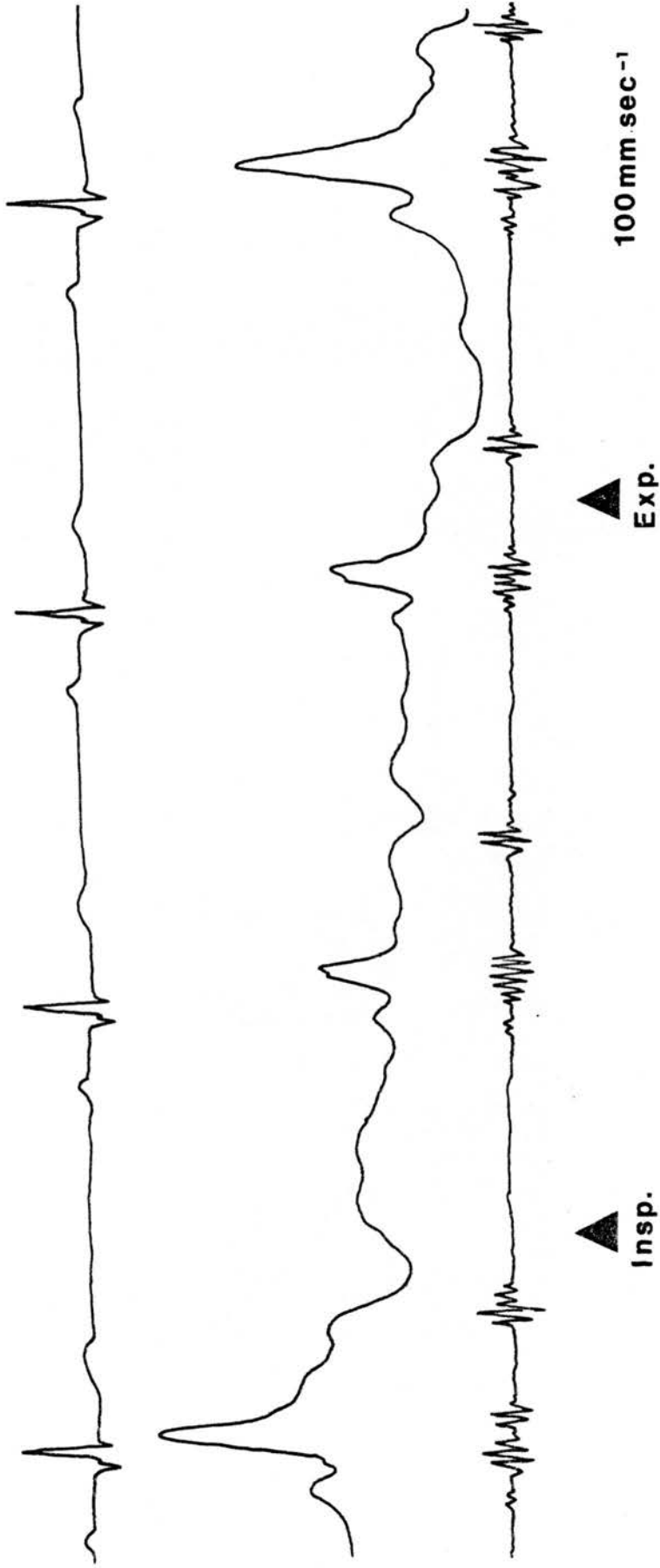
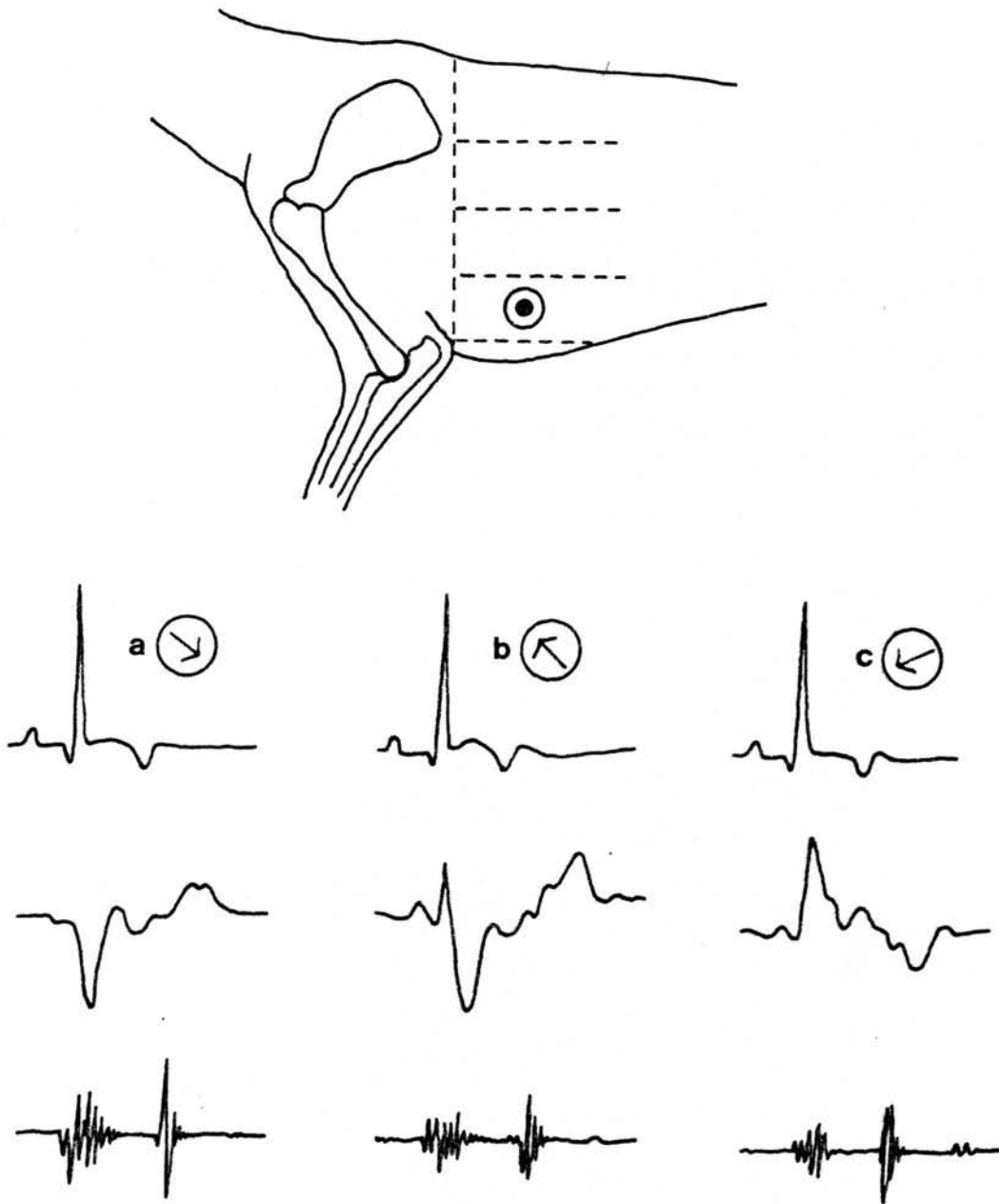


Figure 2.8

Dog No. 4



Angulation of the Transducer to show the variation in waveform from one recording site. Left lateral recumbency - recording from the left side.

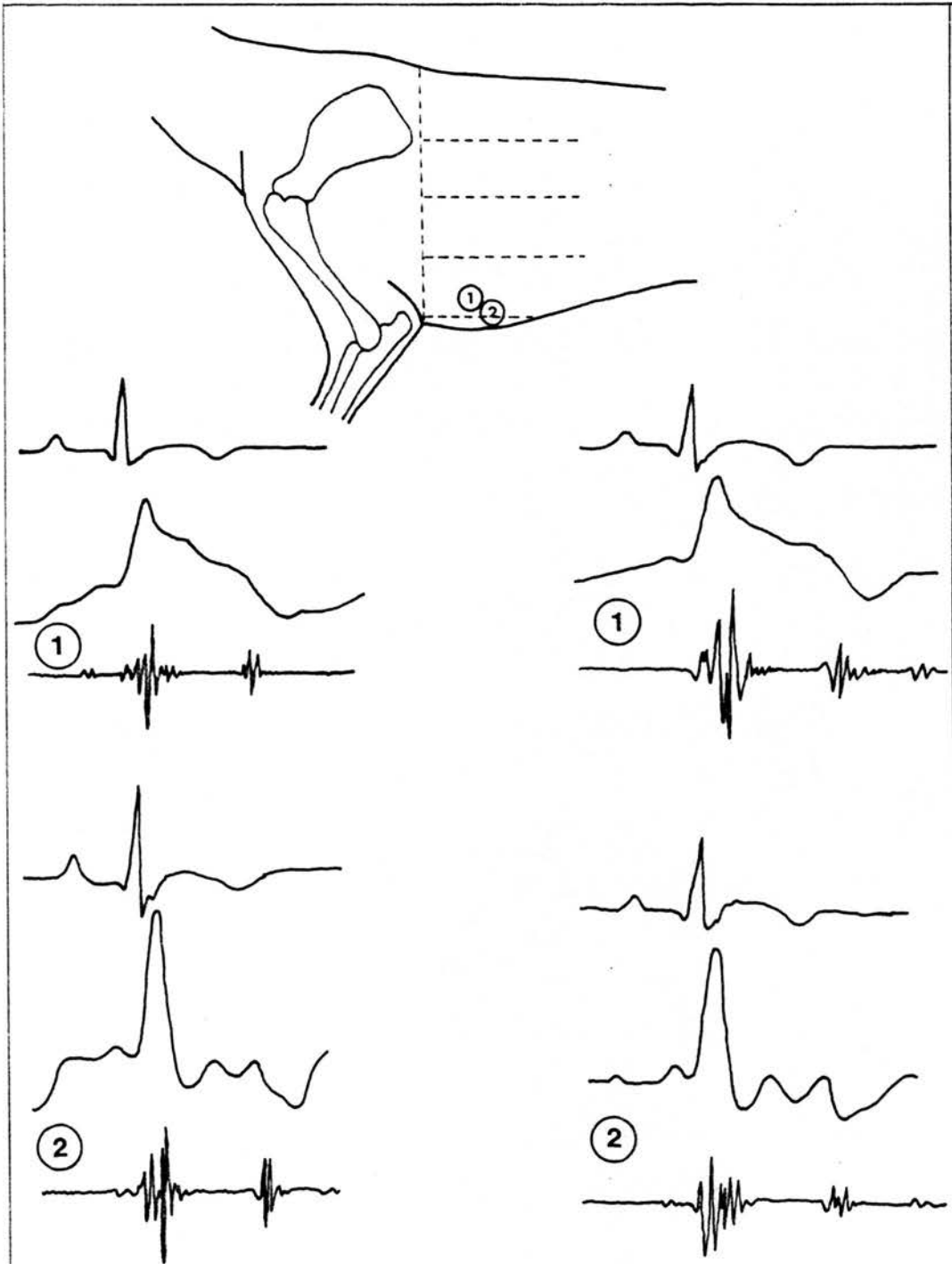


Figure 2.9

Reproduction of the ACG.
Recordings on the right are taken two months after those
on the left. The same waveforms could also be demonstrated
after a three month interval.

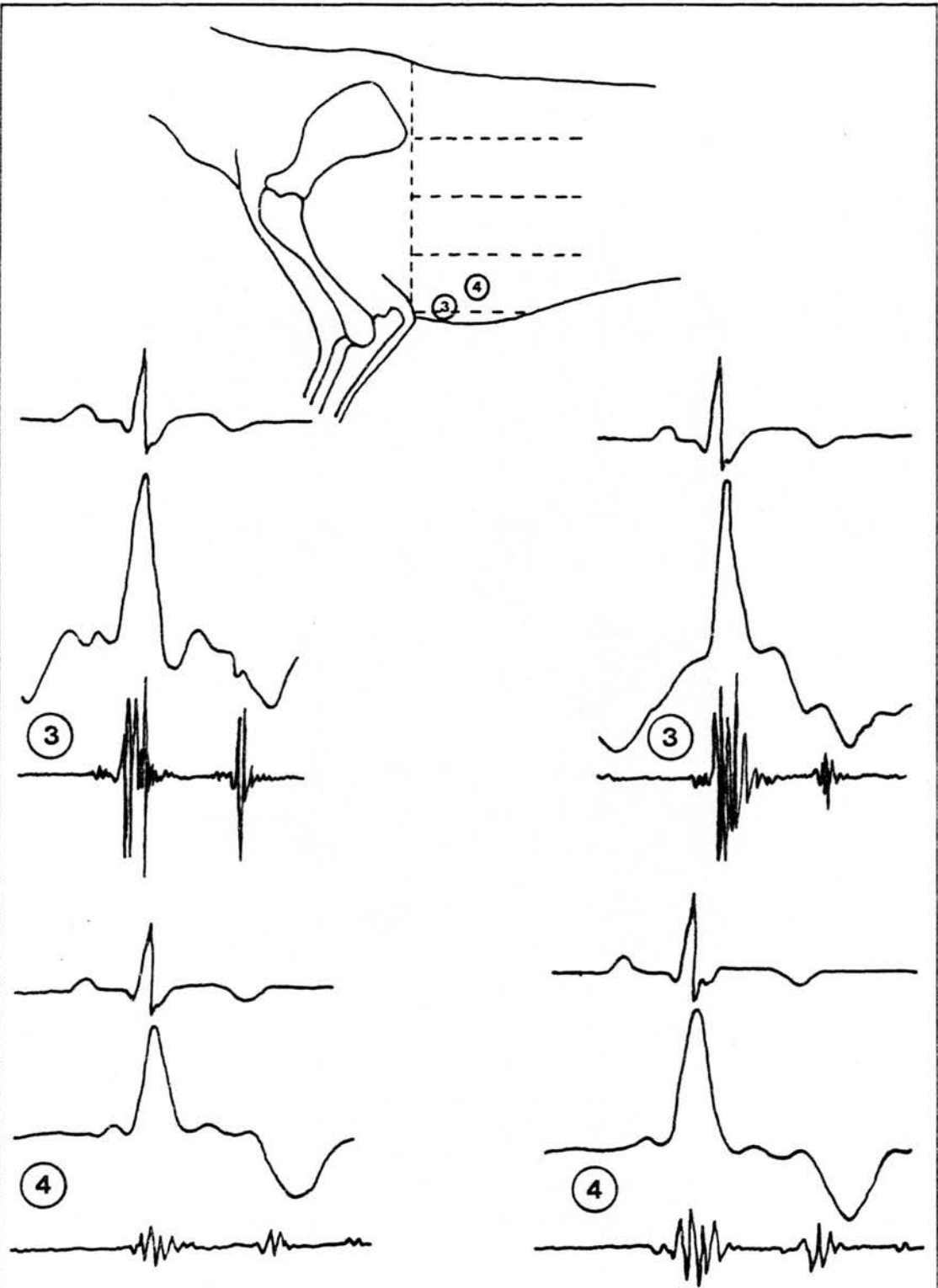


Figure 2.9 (cont'd)

2.4 Discussion

The clarity, amplitude and shape of the apex waveform depend on a number of factors. These experiments have shown that the following points are important when recording an ACG.

Position of the dog:-

Recordings may be made with the anaesthetised dog in left or right lateral recumbency or supported in sternal recumbency. Whatever the position(s) used it is important that the method is standardised. In the interpretation of results the manner in which the position may have influenced the results must be taken into consideration. Although the dog appears to be subject to less postural alterations in blood distribution than man, it is questionable whether the haemodynamics may be altered by placing a dog on one side or the other. Certainly, apexcardiograms from approximately the same area of chest wall with the dog lying on different sides vary considerably. When recording from the side of the dog next to the table, some difficulty was encountered in placing the transducer precisely, due to the confined space. The use of the thick foam on the table helped to alleviate this problem without having to alter the position of the dog.

Position of the transducer on the thoracic wall:-

Covered by its pericardium, the heart extends from the third rib to the cranial border of the sixth rib (Miller, 1964).

Radiographs show variations in position to occur among breeds and individuals, and in the same animal according to age, condition and the presence of pathological processes (Myer and Bonagura, 1982). From our own observations it is interesting to note that there were only slight variations in the position of the maximal impulse between dogs. The strongest vibration on the precordium relates to the motion of the cardiac apex which appears to lie at the level of

the sixth rib in the majority of dogs. Recordings from the apical centre yielded waveforms that were very similar to each other in morphology, displaying the recognised landmarks (see Fig 1.2). In addition, in many dogs the area of maximal impulse was divided by a rib. This often allowed the recording of good quality ACGs, sometimes differing in shape, from either side of the rib.

Once the transducer was moved to the periphery, artefacts appeared in the waveform. The transducer picked up the motion of different areas of myocardium. There may also be a temporal shift within the cycle. Different degrees of artefactual curves were recorded but could be so distorted that they became a mirror image of the normal ACG.

Thoracic Anatomy:-

The heart can be felt to beat more forcibly against the left than the right thorax. The orientation of the heart within the thorax means that ACGs taken at the surface of the left and right sides are referable to different parts of the heart. A longitudinal axis through the heart tips forward from the vertical plane at an angle of about 45° (Sisson and Grossman, 1975). The base is dorso-cranial; the apex points caudo-ventrally where it lies slightly to the left. The caudo-dorsal part of the heart comprises the left atrium and the left ventricle, while the right atrium and right ventricle are cranio-ventral. Although this orientation remains the same through a wide range of breeds, the shape of the thorax varies widely between breeds from the narrow-chested Whippet to the broad width of a Bull Terrier and the brachycephalic breeds. The applicability of apexcardiography to the wide variety of breeds encountered in practice is investigated in Section Four of this thesis. The Beagles used in these experiments had quite varied chest conformation and it was noticed that the breadth of chest in the ventral half affected the recordings, amplitude varying inversely with breadth.

Distance of the heart from the transducer:-

The distance varies with;

- (a) the position of the dog
- (b) the thickness of the chest wall

(a) Position: When a dog is lying in lateral recumbency, gravity causes the transducer, when recording from the uppermost side, to be at a greater distance from the apex and the ventricle wall because they fall away from the rib cage. Recordings from Beagles in the laboratory have, on at least one occasion, shown the highest amplitude on the right, ie uppermost, side in left lateral recumbency. Although the lungs cover most of the surface of the heart, on the right there is a V-shaped notch (Miller, 1964) which allows greater exposure of the heart and might account for the high amplitude. Usually the reverse is true and the strong apex beat, often easily palpable and visible on the chest wall nearest the table requires reduction in amplification for the waveform to be accommodated on the traces.

(b) Thickness of the chest wall: Obesity and emphysema are known to cause a diminution of the signal (Craigie, 1975). The former was a limiting phenomenon in trying to record ACGs in one dog in this section. It was anticipated that in practice this might be a limiting factor in many dogs. However, Gay et al (1978) reported experiences with some obese dogs, including brachycephalics, and suggested that it should be possible to record quality ACGs from most dogs.

Some Beagles had barely visible or palpable apex beats due to the amount of subcutaneous tissue and fat. In these dogs some difficulty was experienced in obtaining a satisfactory shape and size of ACG, but there were no complete failures.

Miscellaneous Factors

Manual pressure applied to the transducer;

Variations in the pressure with which the pick-up head is held against the chest wall causes fluctuations in amplitude and the shape of the apex wave. Unsteady pressure can be responsible for artefacts which may be mistaken for false A waves or hyperdynamic systolic movements. Some attenuation of amplitude occurs if the transducer is held over a rib. Because the transducer relies on sensing a movement between its rim and the centre when it is placed over a rib, there is relative inflexibility and the signal is not strong. Although the variation in amplitude was not accompanied by a change in the time interval, it was considered advisable to moderate the pressure applied to the transducer. The same contour could then be obtained at will in the same dog, the reproducibility of the ACG being most important (Reale, 1967) if serial studies were to be accomplished. The reproducibility of the waveforms appeared to be excellent in these studies.

Respiration;

This has a marked effect on the shape and amplitude of the ACG, distorting the former and depressing the latter. Inspiration, although initiating an outward movement of the chest wall, may cause a depression of the wave. This is explained by the fact that the inspiratory movement does not alter the relationship of the chest wall to the edges of the transducer (Craig, 1975), thus it does not register the total outward movement. At the same time it increased the distance from the heart to the transducer, resulting in a reduction of amplitude. On most inspirations there is over-ranging and the wave is inaccurately recorded. Normal waveforms reappear once the expiratory excursions are complete. Benchimol and Dimond (1963) studied the ACG in human patients and in normal dogs. They recorded a decreased amplitude of the systolic, rapid-filling and A waves during inspiration. An increase in the rapid-filling wave of the left ventricle during expiration was noticed in their tracings.

2.5 Conclusions

The ACG could be recorded from Beagles of varying chest conformation. The best ACG tracings are obtained from the left thorax and the recordings are further enhanced if the dog is laid on this side. The point of maximal apical impulse identifies the location from application of the transducer. Recording outwith this area results in artefacts which may be mistaken, in a clinical situation, for cardiac disease. Recording should take place over several respiratory cycles to minimize the effect this movement has on the trace.

SECTION THREE

CALCULATION OF SYSTOLIC TIME INTERVALS

USING THE APEXCARDIOGRAM

3.1 Introduction

The STI were one of the first quantitative, non-invasive data to be derived in man. Most tests of ventricular performance measure ventricular force and/or distance alone or as a function of time. The STI have time as the only variable (Lewis et al, 1977). Measurements are obtained from simultaneous high speed recordings of any one or all of the following: carotid pulse wave (Weissler, Harris and Schoenfeld, 1968); apexcardiogram (Willems, De Geest and Kesteloot, 1971; Van de Werf et al, 1978); and echocardiogram (Vredevoe, Creekmore and Schiller, 1974; Stephalouros and Witham, 1975; Pipers, Andrysco and Hamlin, 1978), together with ECG and PCG.

The STI vary inversely with heart rate and this must be considered if the results are to be used for comparative studies. The most satisfactory method is to relate the STI to a theoretical zero heart rate. This is obtained by transposition of the terms in the regression equation describing the relationship of STI to heart rate and is known as the STI index (eg. LVETI = left ventricular ejection time index).

STI have been obtained in dogs using invasive techniques (Wallace et al, 1963; Muir and Hamlin, 1973; Gross, Pipers and Hamlin, 1974; Mahler et al, 1975). Tally, Meyer and McNay (1971) evaluated the external PEP in dogs but this was derived by subtracting the LVET which was calculated from internal aortic pressure tracings, from the QS_2 . The echocardiogram has been used to obtain non-invasive STI (Pipers, Andrysco and Hamlin, 1978; Boon, Wingfield and Miller, 1983) but there are relatively few papers concerning the use of the ACG in STI measurements (Willems, De Geest and Kesteloot, 1971; Gabor, Parubszky and Kalman, 1972). Gay et al, (1978) suggest that the ACG should be used as a non-invasive technique for timing left ventricular events.

The aim of the studies recorded in this section was to use the ACG to establish normal STI under anaesthetic and in conscious dogs. The normal values obtained were to form the basis for comparison with dogs with heart disease.

3.2 Materials and Methods

Adult, male Beagles (12.0-22.0 kgs) were used to obtain STI. Normal STI under anaesthetic were recorded in thirty-one dogs. In eighteen dogs, normal STI under anaesthetic were compared with STI in the conscious state. A study of STI following experimentally-produced myocardial ischaemia of three months duration was possible in twenty-two Beagles.

3.2.1 Anaesthetic Procedure

A sterile, 19G, vein set was introduced into the right cephalic vein to facilitate administration of premedication, anaesthetic and fluid therapy, if required. Anaesthetic, with acetylpromazine at a dose of 0.2 mg/kg i.v., was followed by induction of general anaesthetic with pentobarbitone sodium at 25-30 mg/kg i.v. Intubation with a cuffed endotracheal tube completed the anaesthetic procedure.

3.2.2 Recording Technique

Recording commenced after about 15 minutes, in which the dog's heart rate and respiration were allowed to stabilize under anaesthetic. The animal was laid in left lateral recumbency in a sound-proofed room and ECG recordings of the Einthoven limb leads (I, II, III) and the augmented unipolar leads (aVR, aVL, aVF) were made. An oscilloscope was used to monitor the simultaneous recordings of the ECG, ACG and PCG. The Pulse Phono Transducer (Section 2.2.2) was held manually against the shaved left lateral thorax at the point of maximal palpable impulse as in Section 2.2.3. The gain on the preamplifier was adjusted to obtain the optimum amplitude,

without causing over-ranging. If all traces yielded clear information and the ACG was of the correct polarity (Section 2.4), then a permanent recording was made over at least four respiratory cycles. A minimum of three recordings were taken over a thirty minute period at paper speeds of 25, 50, 100 and 250 mm sec⁻¹.

After this recording, the dogs were submitted to experimentally - produced left ventricular ischaemia by ligation of the left anterior descending (LAD) artery (Alps, Calder, Wilson and Scott-Park, 1983). The recordings were repeated in twenty-two dogs following a three month recovery period.

3.2.3 Recording Procedure in Conscious Dogs

Several visits to the sound-proofed recording room, prior to data collection, allowed animals to become familiar with the operations and the equipment. Each dog was placed in left lateral recumbency using gentle restraint. The technique used was identical to that described in Section 3.2.2. Data collection was stopped if the dog became restless or began to pant. The maximum time for recording in the same position was fifteen minutes. A short break could be followed by a further ten minutes of recording before returning the animal to its kennel.

3.2.4 Analysis of Simultaneous Recordings

The recordings from each dog was examined and traces which clearly demonstrated the necessary landmarks (vide infra) were used to assimilate data. All intervals were calculated as the mean of measurements on five consecutive cycles, the RR intervals of which did not vary by more than 10 msec. Traces taken at 100 mm sec⁻¹ were accurate to the nearest 5 msec. Heart rate and the RR intervals were recorded from the trace.

The intervals measured were: QS_2 - from the Q wave of the ECG to the aortic component of the second heart sound on the PCG. Q-C - the Q wave of the ECG to the C point (start of the systolic upstroke) on the ACG. SUT - the C point to the E point (the peak of the ACG) on the ACG. $PEP = Q-C + SUT$. $LVET = QS_2 - PEP$. The first derivative of the ACG - dA/dt gave two intervals: $t - dA/dt$ - from the start of the upstroke of dA/dt to its peak. $Q-dA/dt$ - from the Q wave of the ECG to the peak dA/dt .

The data were transferred to graphs which demonstrated the relationship of STI to the instantaneous heart rate (HR). This was obtained by dividing 60,000 by the RR interval to give the HR. The STI were plotted on the ordinate as the dependent variable, against the independent variable, HR, on the abscissa.

A linear regression line was fitted using the method of least squares and the correlation co-efficient calculated to assess the closeness of fit between the HR and STI. The calculation of the correlation co-efficient (r) was made as follows:

$$r = \frac{\sum (X - \bar{X}) (Y - \bar{Y})}{\sqrt{\sum (X - \bar{X})^2 \sum (Y - \bar{Y})^2}}$$

With X representing the heart rate and Y representing the STI. The calculation was made to six decimal places and the result given to two decimal places. To test the deviation of r from 0, or nil correlation, a t - test was used in the following calculation:

$$t = r \sqrt{\frac{n - 2}{1 - r^2}}$$

The t table being entered at $n - 2$ degrees of freedom. An arbitrary level of $P > 0.05$ was taken to imply no statistical significance.

The equation describing the regression of Y on X is given by:

$$Y = a + bX$$

Where $a = Y$ intercept and $b =$ gradient of the line. The formulae are as follows:

$$b = \frac{\sum(X - \bar{X})(Y - \bar{Y})}{\sum(X - \bar{X})^2} \quad a = \bar{Y} - b\bar{X}$$

Computer programs (Appendix 4) were written to deal with the data which were too numerous to compute on a calculator.

To establish whether there was any difference between paired observations (eg. STI before and after anaesthesia), the null hypothesis (that there was no difference between them) was erected. The standard error of difference between the means was established, using the formula:

$$SE \text{ Diff} = \sqrt{\frac{SD^2}{n_1} + \frac{SD^2}{n_2}}$$

Where SD = standard deviation calculated by:

$$SD = \sqrt{\frac{\sum(X - \bar{X})^2}{n - 1}}$$

The difference between means was divided by the SE difference to establish how many multiples of its standard error this difference represents. If the result was greater than, or equal to, the 1% probability level, then the difference between the means was considered statistically significant.

3.2.5 Division of Dogs into Groups

Group A : normal, anaesthetised dogs. The STI data presented are from 31 dogs. A total of 93 measurements (each measurement is the average over five consecutive beats) were taken for each STI on one occasion (see Section 3.2.2)

Group B : STI data are presented from 18 normal dogs. The recordings were taken prior to, and during anaesthesia. Eleven of these dogs were from Group A, five dogs were those used for the explorative work reported in Section 2, and two dogs were used in an initial assessment of the recording of ACGs in conscious dogs. A total of 73 measurements before anaesthesia and 60 measurements during anaesthesia were made in the same 18 dogs.

Group C : all 31 dogs in Group A underwent surgery to ligate the left anterior descending coronary artery. Eight dogs died following, probably as a result of the ligation, which left 23 dogs available for post-ligation STI measurement. Recordings from one of these dogs were not of sufficient quality for STI measurement and so the results present data from 22 dogs. A total of 72 measurements were made, under anaesthesia.

3.3 Results

Recordings of the ECG, PCG and ACG were obtained from all dogs in the study. Not all the recordings made were of sufficient quality for analysis. This was usually because either the ACG, or the PCG or both, did not clearly demonstrate the landmarks used for STI measurement.

Futhermore, although the dA/dt was recorded the two intervals, t - peak dA/dt and Q - dA/dt could not be consistently measured over five consecutive heart beats in many recordings. Not only was the peak of the differential wave often incomplete, but the measurements obtained varied widely from beat to beat.

3.3.1 Data from Group A Dogs

The STI data from 31 normal anaesthetised dogs are demonstrated graphically in Fig 3.1 (a) - (e). The plot of QS_2 vs. instantaneous HR (Fig 3.1 a) measured from anaesthetised dogs shows that a clear inverse relationship exists between HR and QS_2 . A similar inverse relationship exists between HR and LVET (Fig 3.1 b). The correlation of PEP with HR (-0.39) indicates a weaker relationship between these two variables but the slope of the regression (-0.13) differs significantly ($p < 0.001$) from zero (Fig 3.1 c). The regression and correlation of PEP reflect the summation of the two sub-intervals, Q-C and SUT. In normal, anaesthetised dogs Group A, only the SUT demonstrates a significant ($P < 0.001$) linear relationship with HR.

Figure 3.1 (a) - (e) : STI Obtained from Group A
(normal anaesthetised dogs)

(a) - QS_2

(b) - LVET

(c) - PEP

(d) - Q-C and SUT

(e) - PEP/LVET

In all graphs the linear regression equation and the correlation co-efficient (r) is stated and the line relating HR and individual STI is drawn.

Figure 3.1 (a)

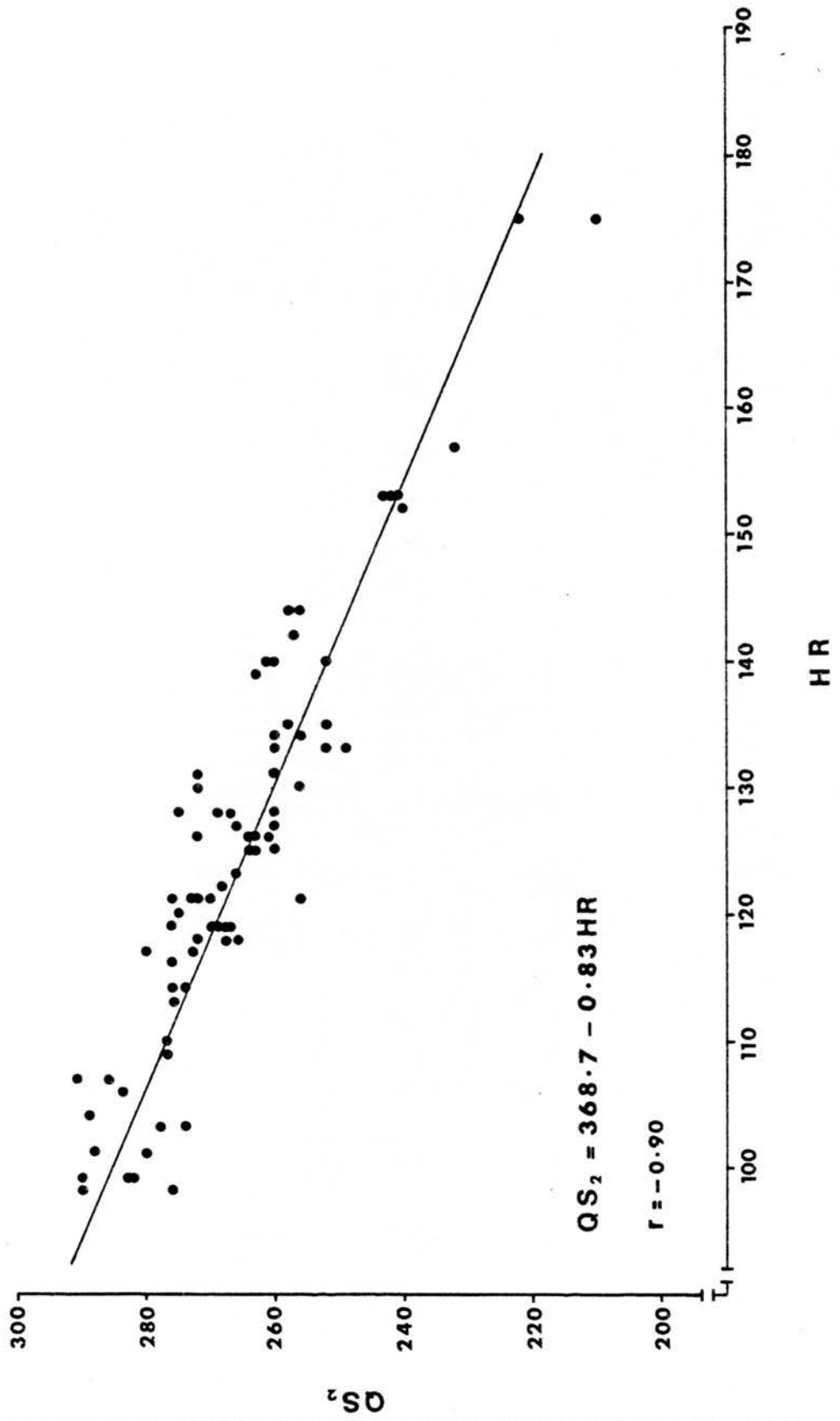


Figure 3.1 (b)

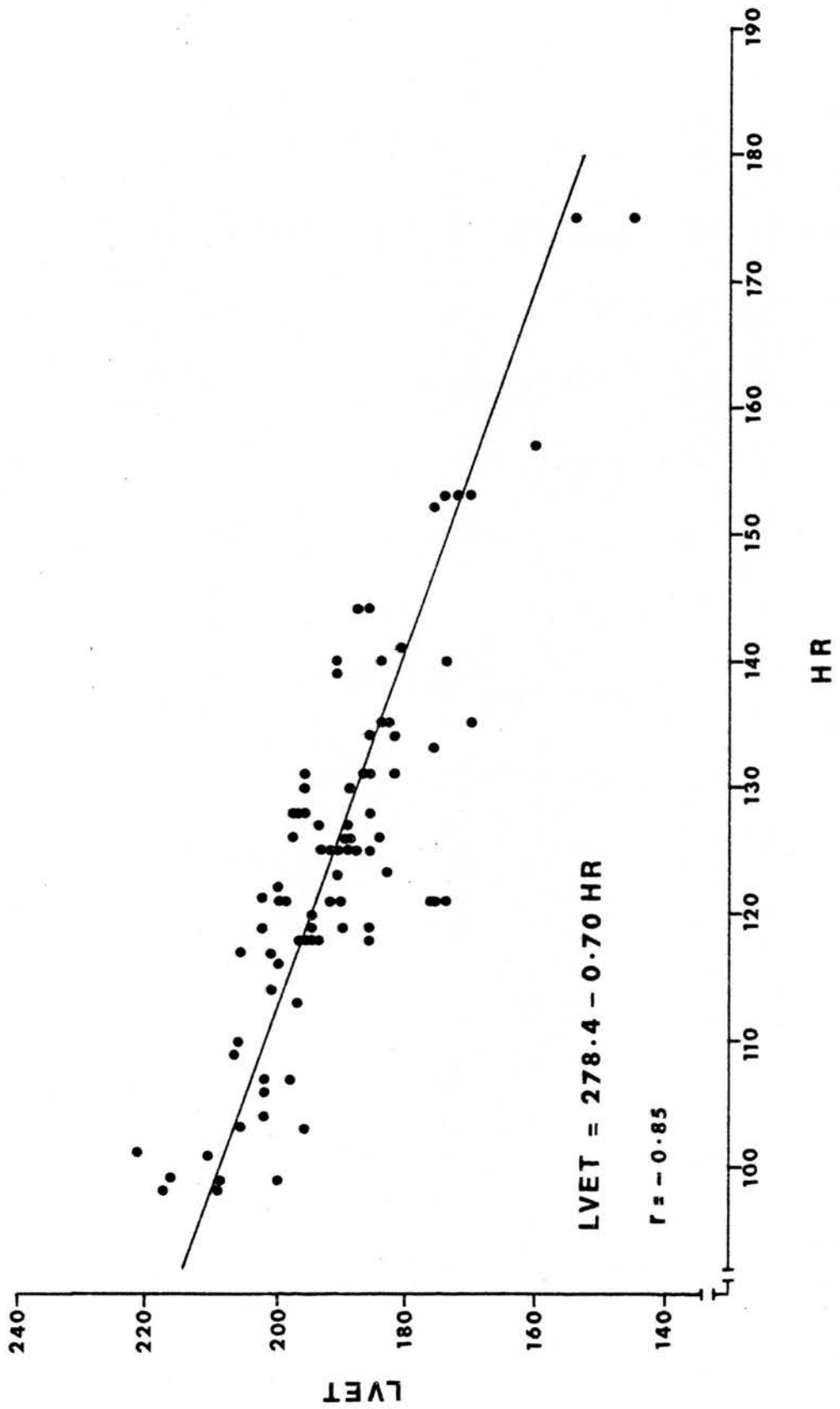


Figure 3.1 (c)

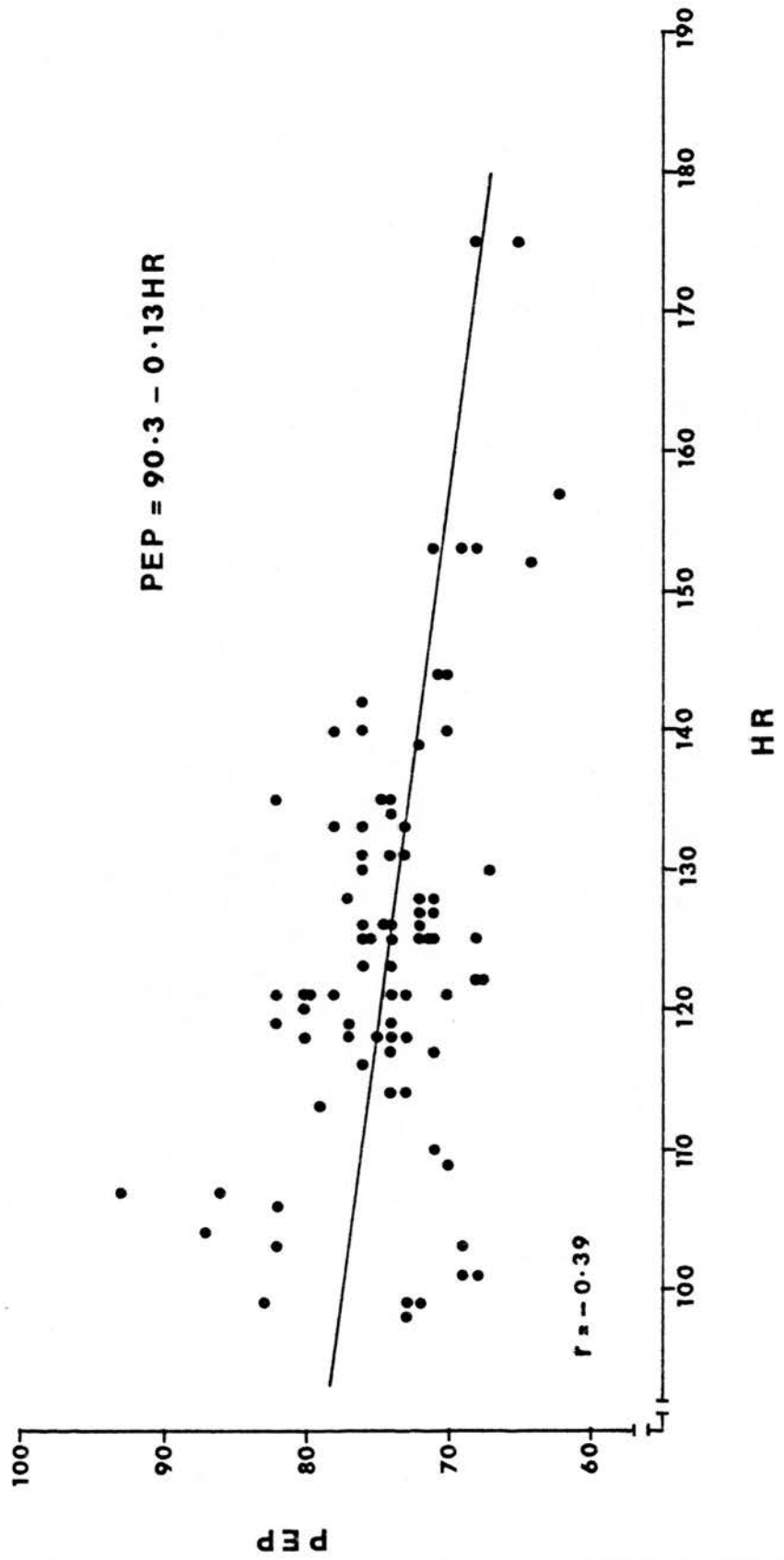


Figure 3.1 (d)

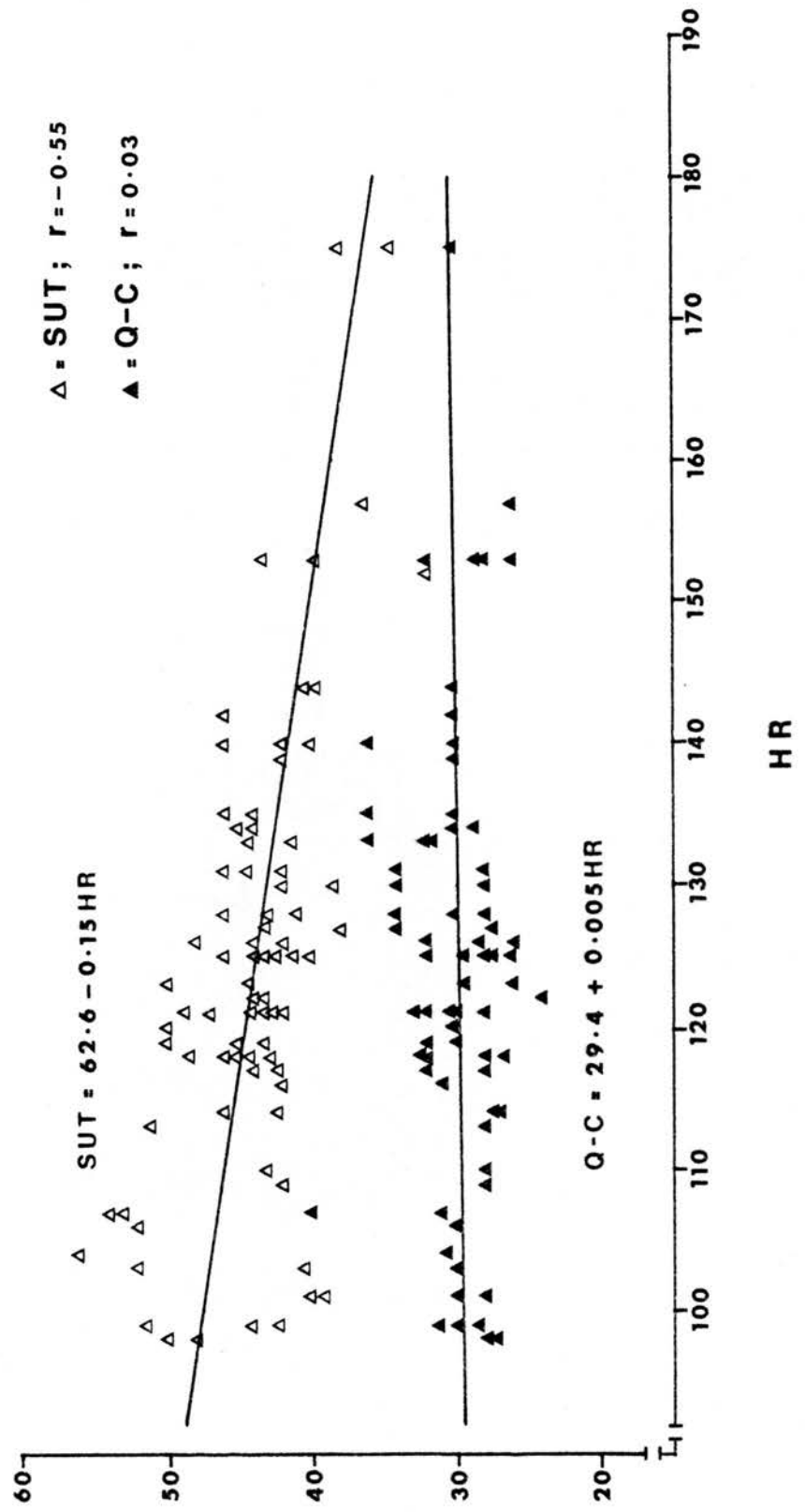
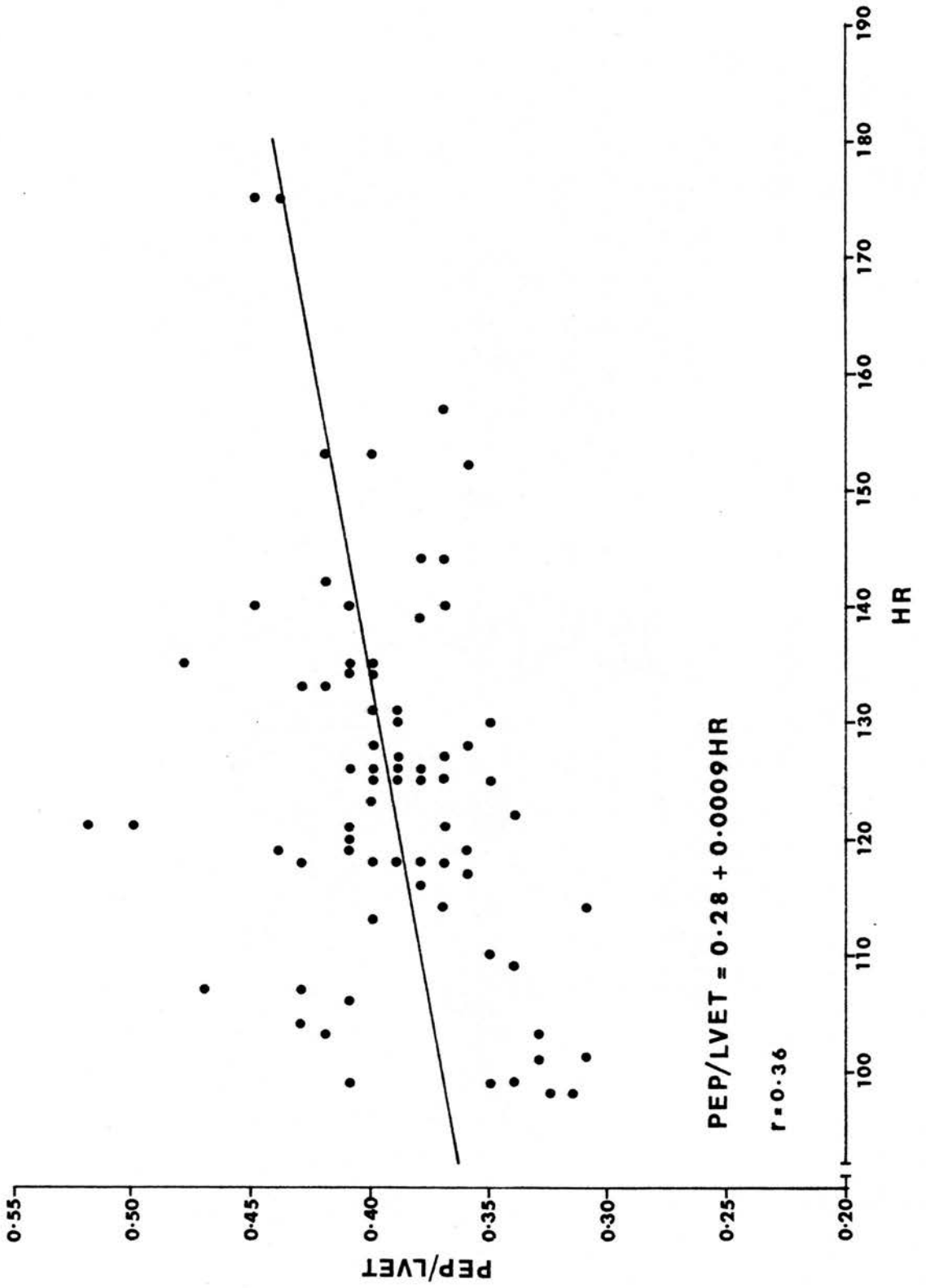


Figure 3.1 (e)



The ratio PEP/LVET shows a significant positive correlation with HR.

The relationship in normal dogs between heart rate and the duration of the phases of left ventricular systole under anaesthesia are summarized in Table 3.1.

Table 3.1 : STI Regression Data from Group A Dogs (normal, anaesthetised)

<u>Systolic Interval</u>	<u>Regression equation</u>	<u>S.D.</u>	<u>Correlations</u>	
QS ₂	368.7 - 0.83 HR	13.62	-0.90	P<0.001
LVET	278.4 - 0.70 HR	12.29	-0.85	P<0.001
PEP	90.3 - 0.13 HR	4.93	-0.39	P<0.001
Q-C	29.4 - 0.005 HR	2.61	0.03	N.S.
SUT	62.6 - 0.15 HR	4.03	-0.55	P<0.001
PEP/LVET	0.28 - 0.0009 HR	8.50	0.36	P<0.001

All intervals are expressed in milliseconds. S.D = sample standard deviation from regression in milliseconds. The significance of the regression co-efficients is expressed in the last column. N.S. = not statistically significant. (Section 3.2.4)

3.3.2 Data from Group B Dogs

Values for QS₂ from both anaesthetised and conscious dogs show a similar inverse relationship with HR (Fig. 3.2 a). The slopes of both lines (-0.54 and -0.75) differ significantly from zero but the regression equations are significantly different (P<0.001) from each other. The plots of LVET vs HR measured from anaesthetised and conscious dogs show a clear inverse relationship exists between ejection time and HR. (Fig 3.2 c)

Figure 3.2 (a) - (f)

Comparison of STI from Group B Dogs (before and during anaesthesia).

- (a) - QS_2
- (b) - PEP
- (c) - LVET
- (d) - PEP/LVET
- (e) - Q-C and SUT from anaesthetised dogs
- (f) - Q-C and SUT from conscious dogs

In all graphs except Fig 3.2(e) and(f), the STI values obtained from conscious and anaesthetised dogs are displayed on the same graph.

In Fig 3.2(e) and (f) Q-C and SUT are represented on the same graph. For clarity, a separate graph for each set of values (anaesthetised and conscious) is presented.

Figure 3.2 (a)

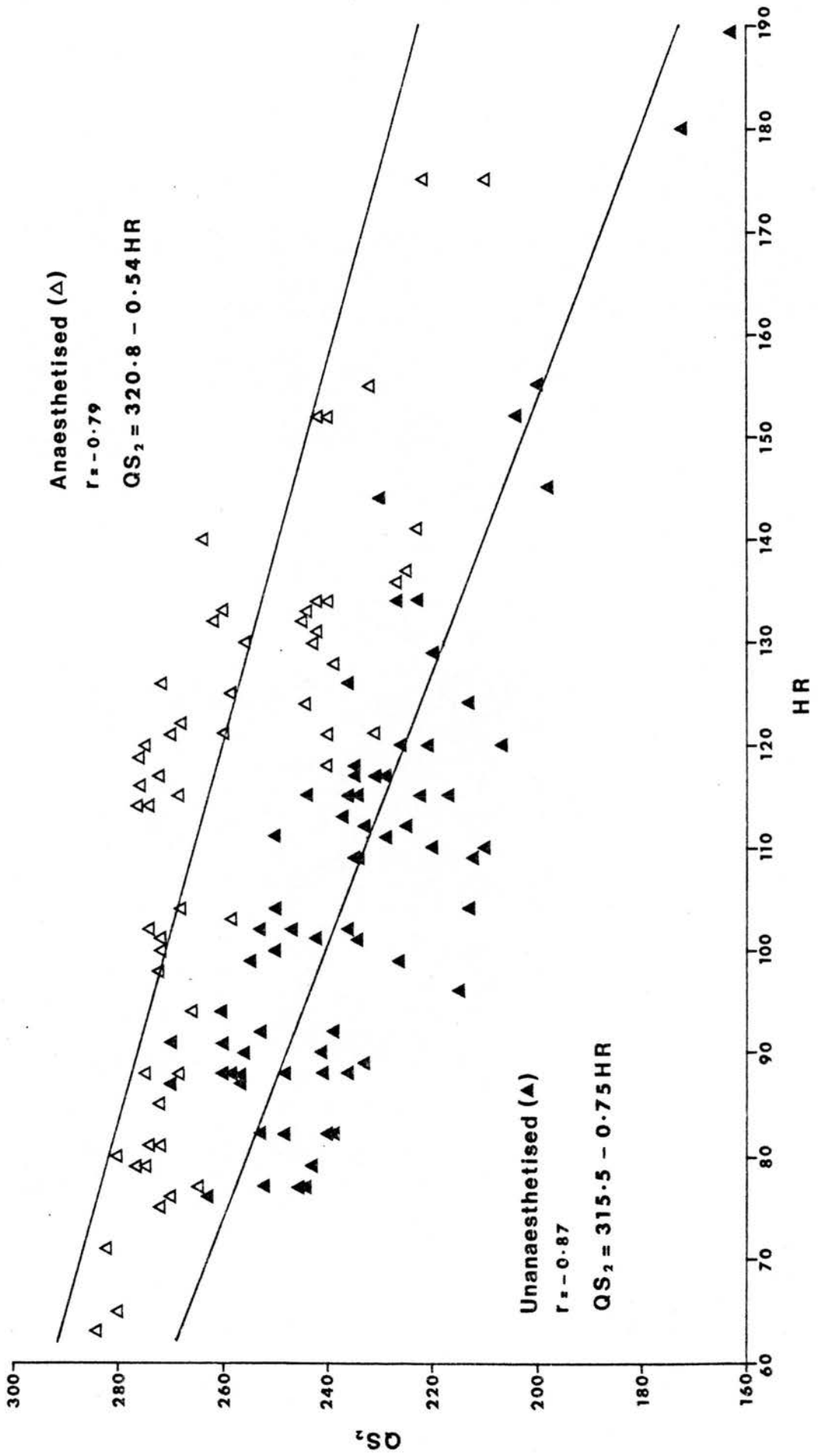


Figure 3.2 (b)

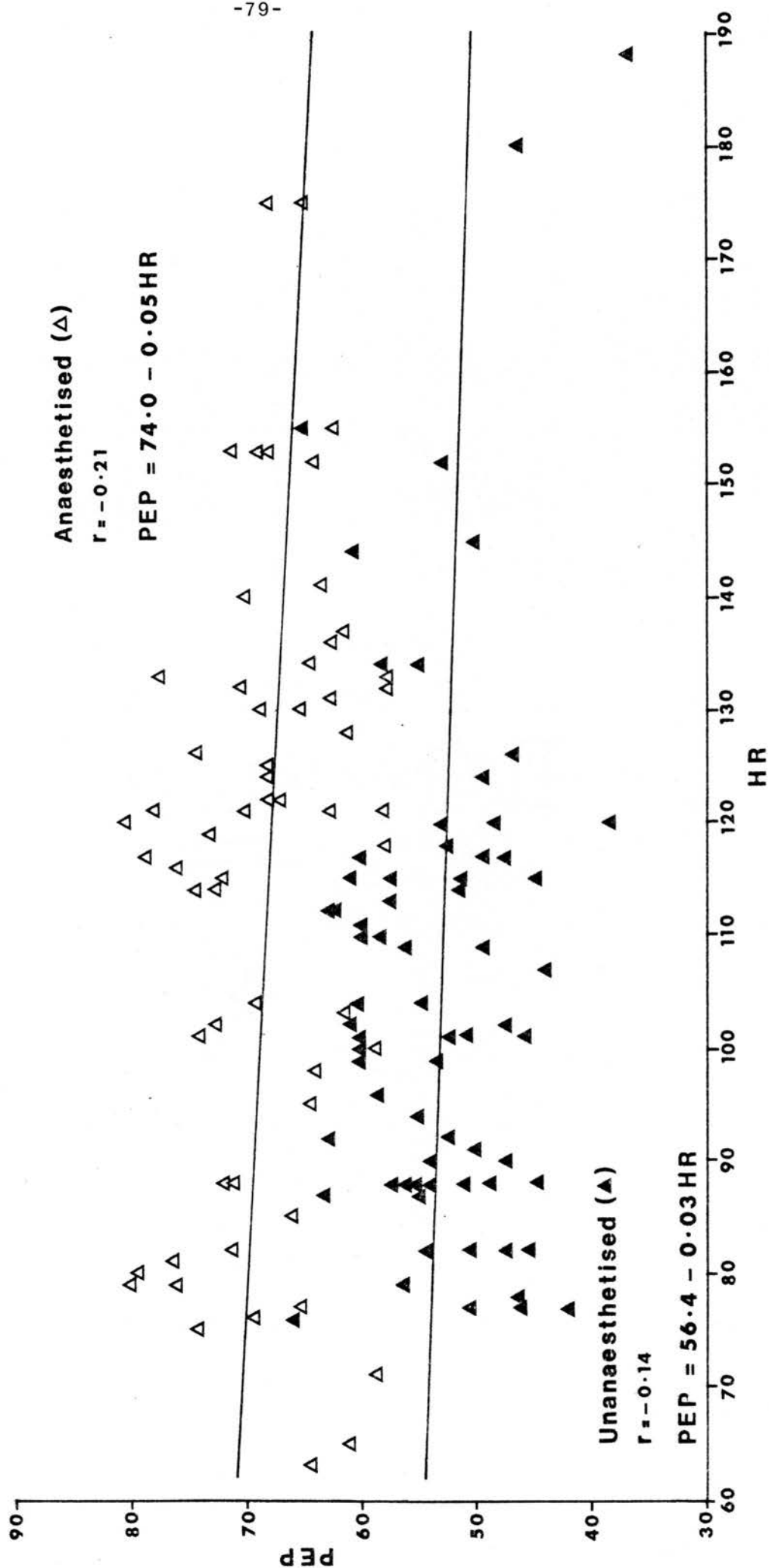


Figure 3.2 (c)

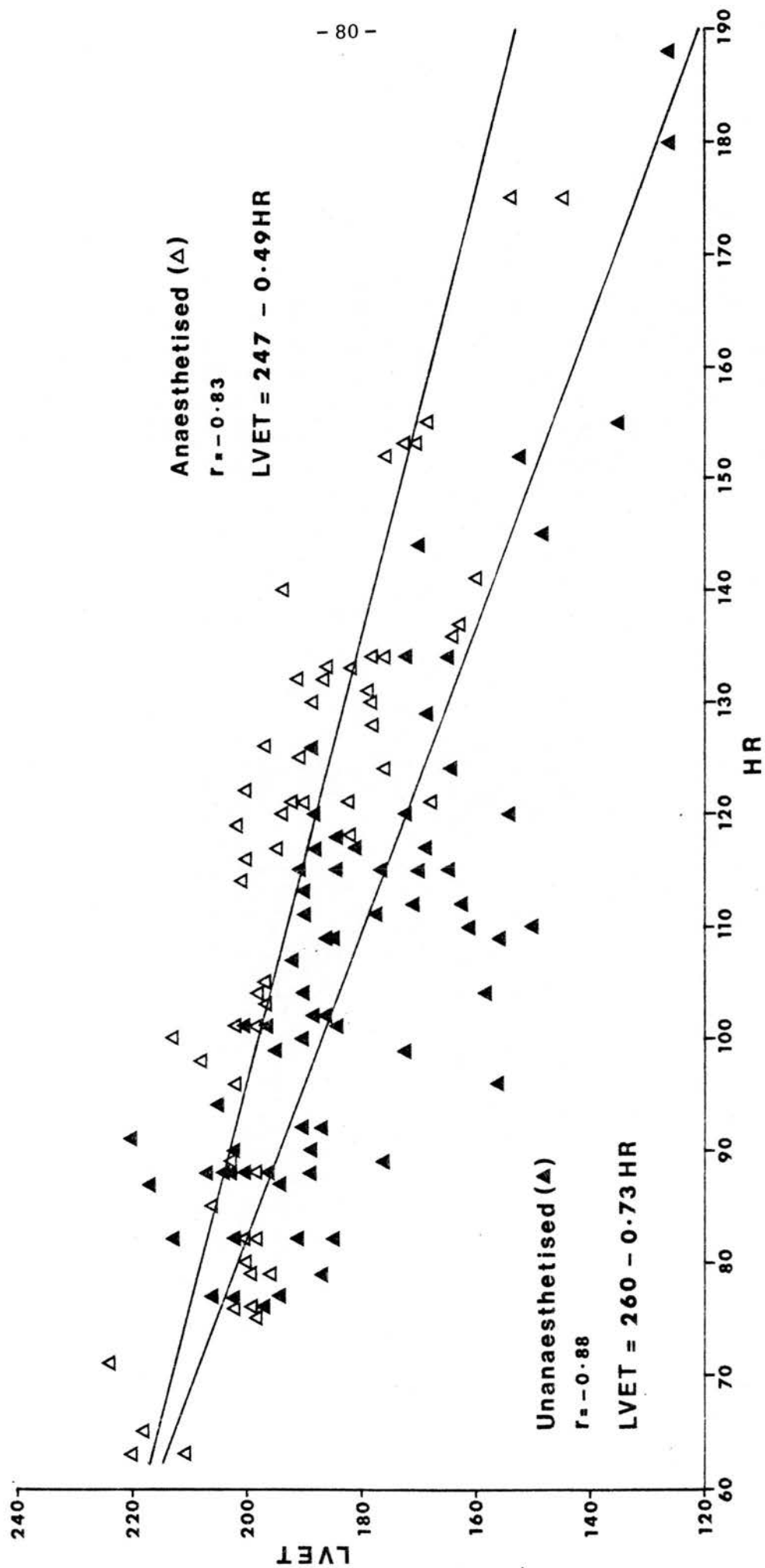


Figure 3.2 (d)

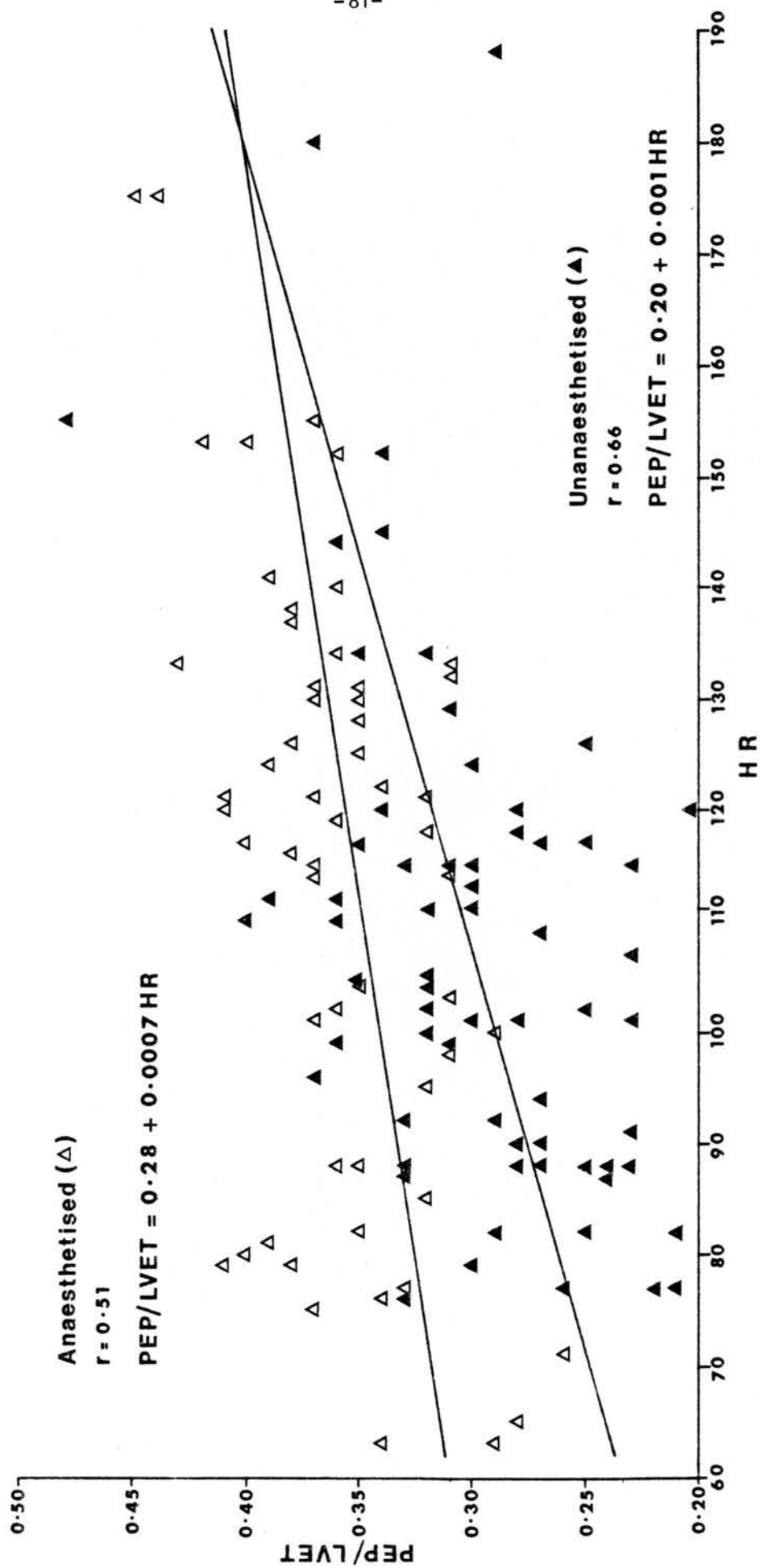


Figure 3.2 (e)

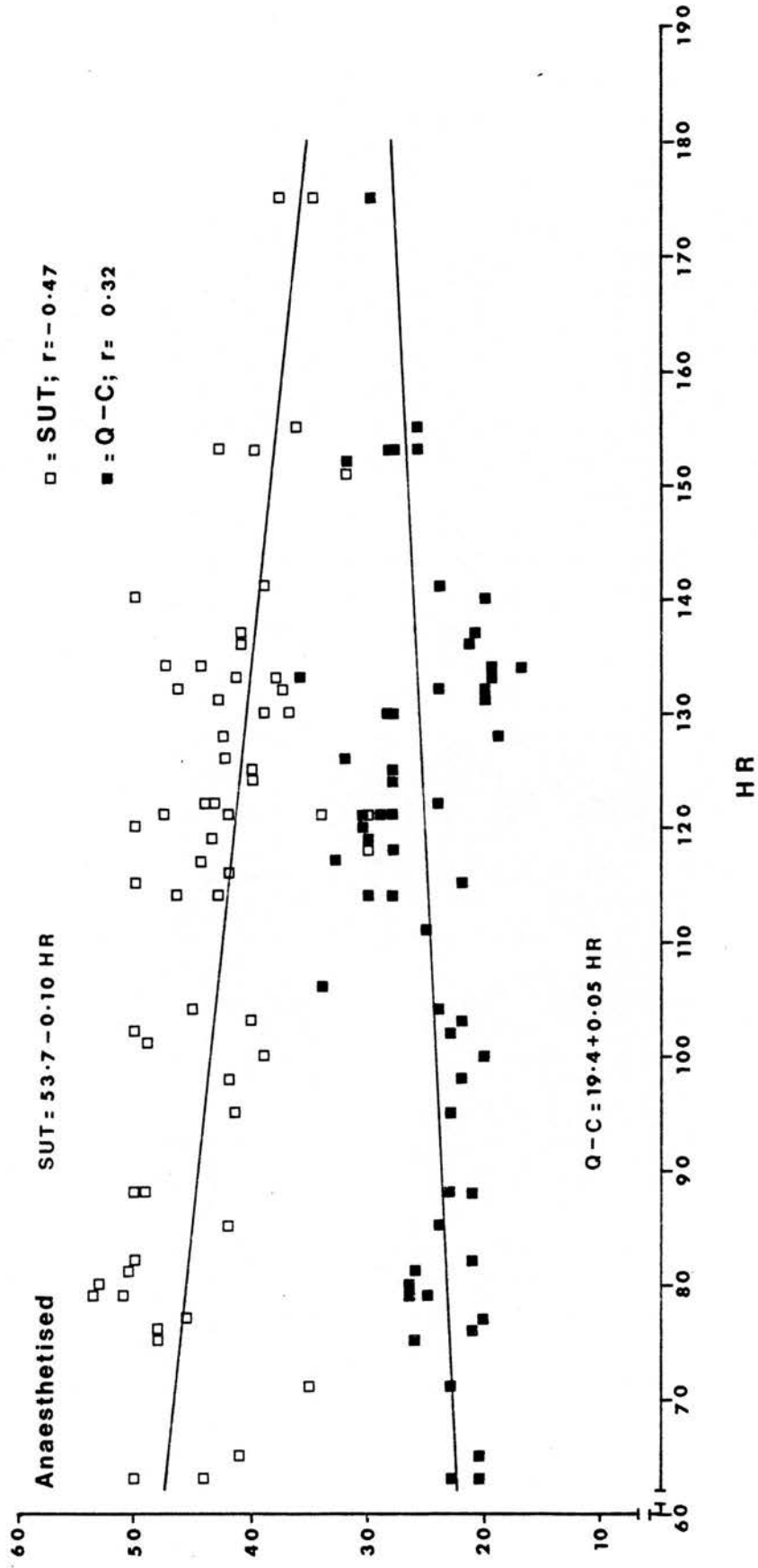


Figure 3.2 (f)

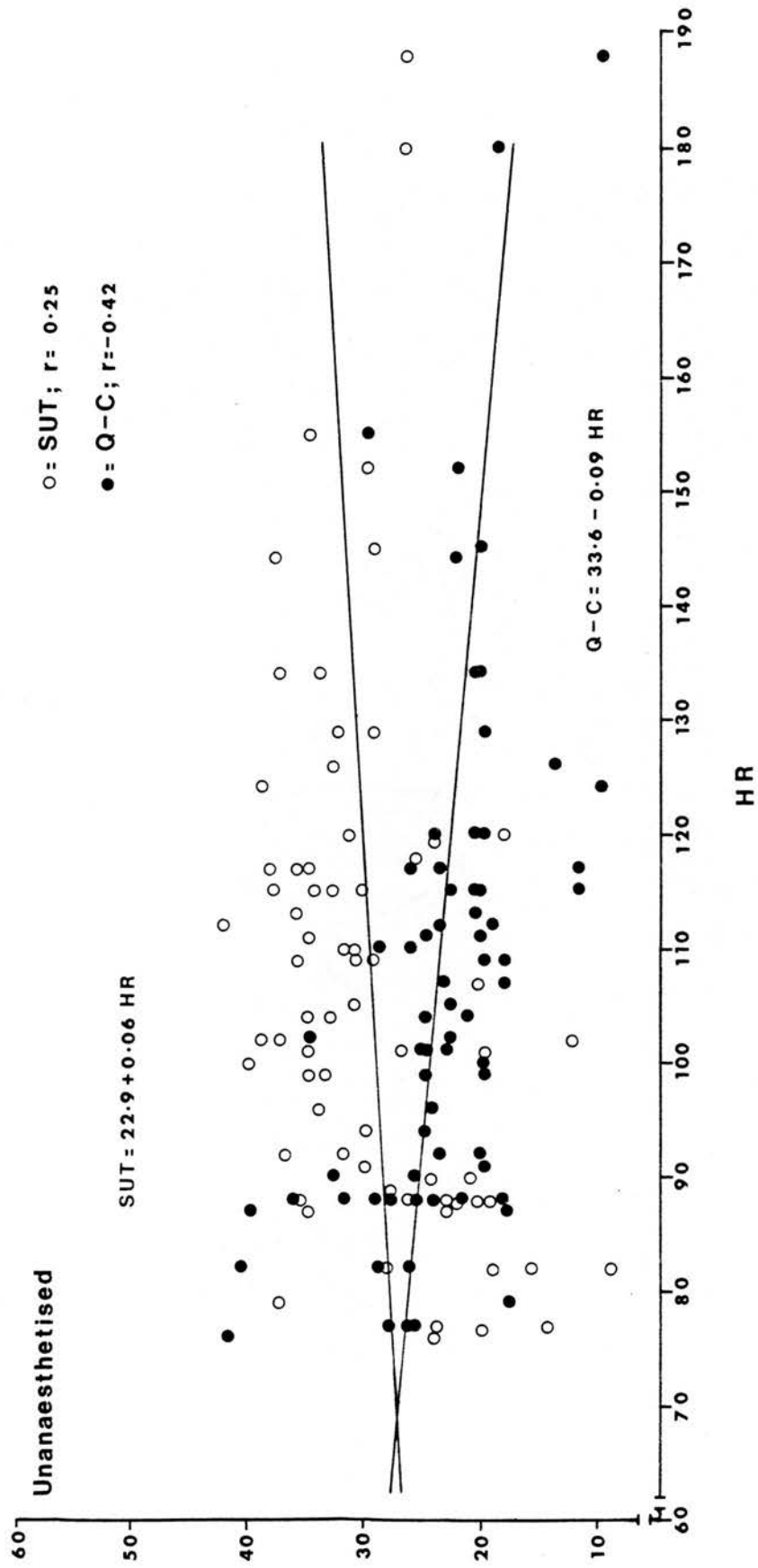


Table 3.2 : STI Regression Data from Conscious Dogs (Group B)

					<u>S.D.</u>	<u>Correlation</u>	
QS ₂	=	315.5	- 0.75 HR	24.95	-0.88		P<0.001
LVET	=	260.0	- 0.73 HR	24.82	-0.87		P<0.001
PEP	=	56.4	- 0.03 HR	6.15	-0.14		N.S.
Q-C	=	33.6	- 0.09 HR	6.19	-0.42		P<0.001
SUT	=	22.9	+ 0.06 HR	7.16	0.25		P<0.02
PEP/ LVET	=	0.20	+ 0.001 HR	0.06	0.66		P<0.001

Table 3.3 : Comparison of STI from Group B Dogs

	<u>Anaesthetised</u>	<u>Conscious</u>	
QS ₂	= 320.8 - 0.54 HR	= 315.5 - 0.75 HR	Signif. Diff. P<0.001
LVET	= 247.0 - 0.49 HR	= 260.0 - 0.73 HR	Signif. Diff. P<0.001
PEP	= 74.0 - 0.05 HR	= 56.4 - 0.03 HR	Signif. Diff. P<0.001
PEP/ LVET	= 0.20+ 0.0007 HR	= 0.20+ 0.001 HR	Signif. Diff. P<0.01

The slopes (-0.49 and -0.73) differ significantly from zero and from each other ($P < 0.001$). The PEP in conscious dogs does not demonstrate a relationship with instantaneous HR ie. the slope of the line (-0.03) does not differ significantly from zero. The values for PEP in anaesthetised and conscious dogs differ significantly from each other. (Fig 3.2 c) The Q-C and SUT in conscious dogs each demonstrated a regression line opposite in sign to that recorded in anaesthetised dogs but both intervals were, on average, lower in conscious dogs. (Fig 3.2 e) compared with Fig 3.2 f). The PEP/LVET demonstrated a positive, significant ($P < 0.001$) correlation with HR in both anaesthetised and conscious dogs (Fig 3.2 d). The difference between the groups was not so marked ($P < 0.01$). The anaesthetised values were, on average, higher.

In conclusion, for QS_2 , LVET and PEP are longer during anaesthesia when compared to with those for conscious dogs. The same is true of SUT, while Q-C demonstrates a less obvious increase during anaesthesia. PEP/LVET is less affected by anaesthesia but the ratio is on average higher during anaesthesia. The information is summarized in Tables 3.2 and 3.3.

The regression equations derived from the dogs in Group A were not identical to those calculated for the STI values from anaesthetised dogs in Group B. These differences are stated in Table 3.4.

Table 3.4 : STI from Anaesthetised Dogs - A comparison between Group A (n = 31) and Group B (n = 18)

<u>Group A</u>	<u>Group B</u>	
$QS_2 = 368.7 - 0.83 \text{ HR}$	$= 320.8 - 0.54 \text{ HR}$	Signif. Diff. $P < 0.001$
$LVET = 278.4 - 0.70 \text{ HR}$	$= 247.0 - 0.49 \text{ HR}$	Signif. Diff. $P < 0.001$
$PEP = 90.3 - 0.13 \text{ HR}$	$= 74.0 - 0.05 \text{ HR}$	N.S.
$PEP/ LVET = 0.28 - 0.0009 \text{ HR}$	$= 0.20 + 0.0007 \text{ HR}$	Signif. Diff. $P < 0.001$

3.3.3 Data from Group C (Dogs after coronary artery ligation)

The data from this group are presented graphically in Fig 3.3 (a) - (e). The regression lines derived from these dogs before anaesthesia (Group A) are superimposed (Dotted lines) on these graphs. The regression data for Group C is summarized in Table 3.5 and Table 3.6 shows the relationship between the normal regression data and the regression data derived from dogs, three months post-ligation.

The STI showed no significant differences from the normal values obtained prior to surgery (Table 3.1)

Figure 3.3 (a) - (e)

STI obtained from Group C Dogs : (after coronary artery ligation)

(a) - QS_2

(b) - LVET

(c) - PEP

(d) - Q-C & SUT

(e) - PEP/LVET

In all graphs, the regression line for Group C STI is drawn (continuous line) and for comparison, the normal regression line for these dogs (Group A) is superimposed (dotted line).

Figure 3.3 (a)

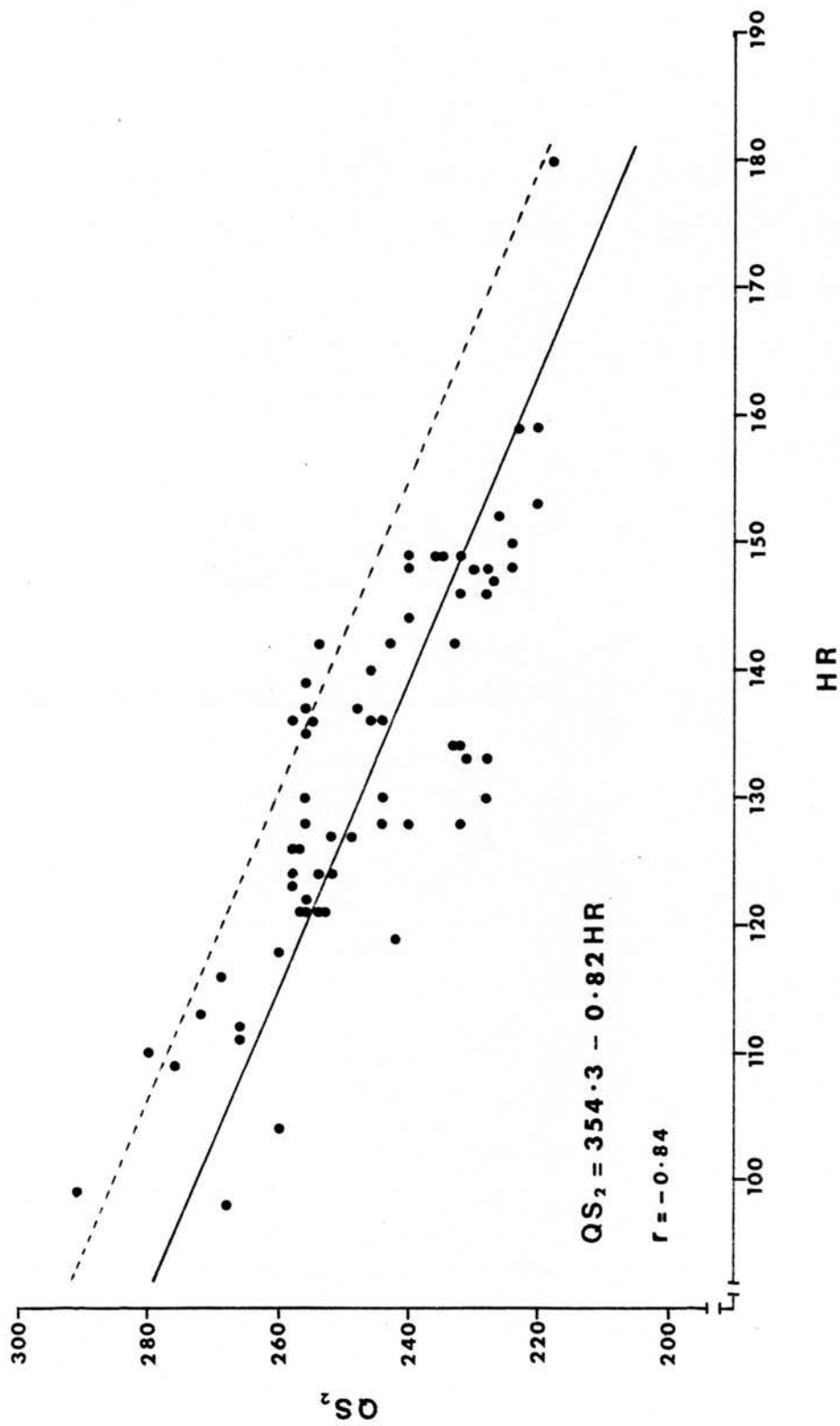


Figure 3.3 (b)

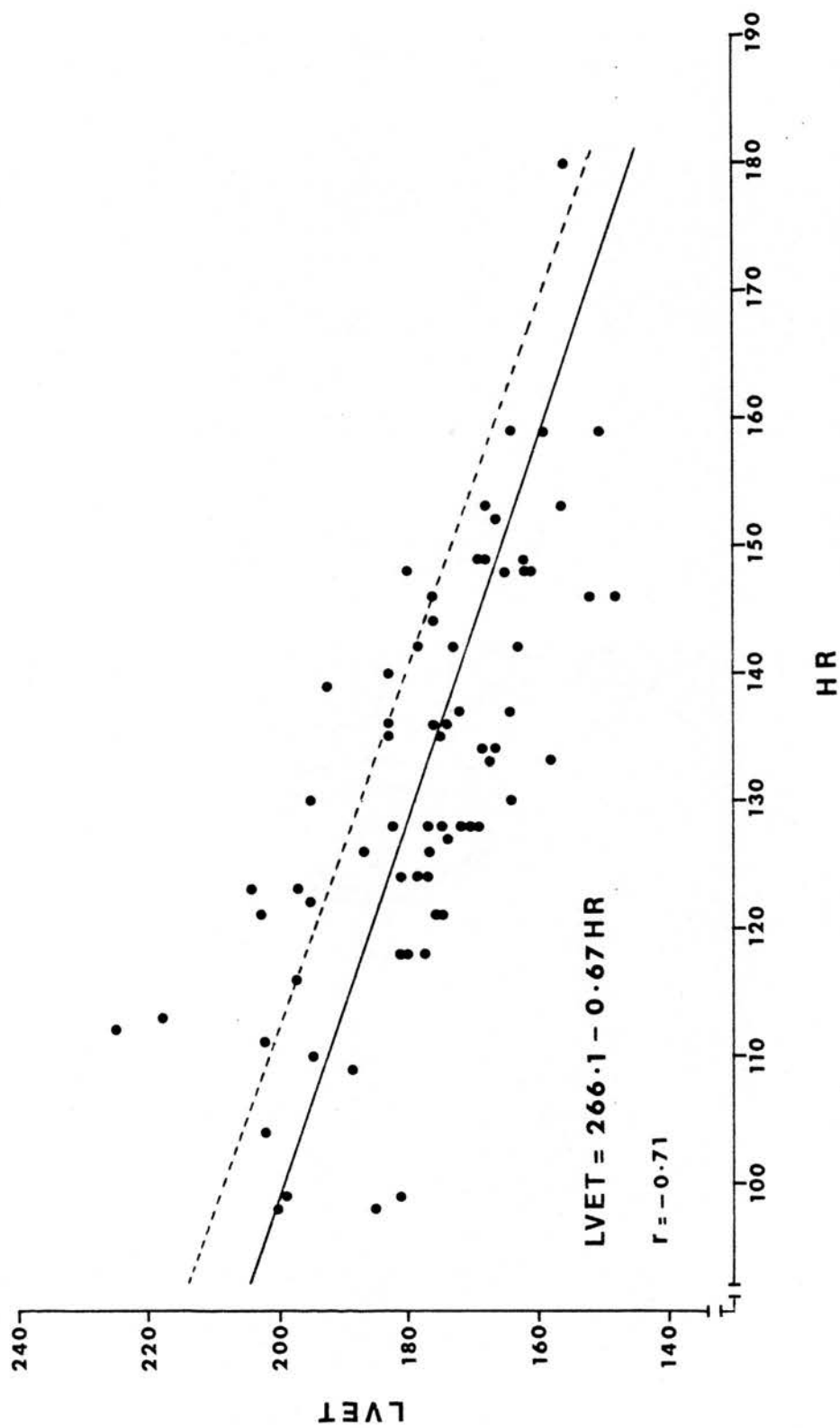


Figure 3.3 (c)

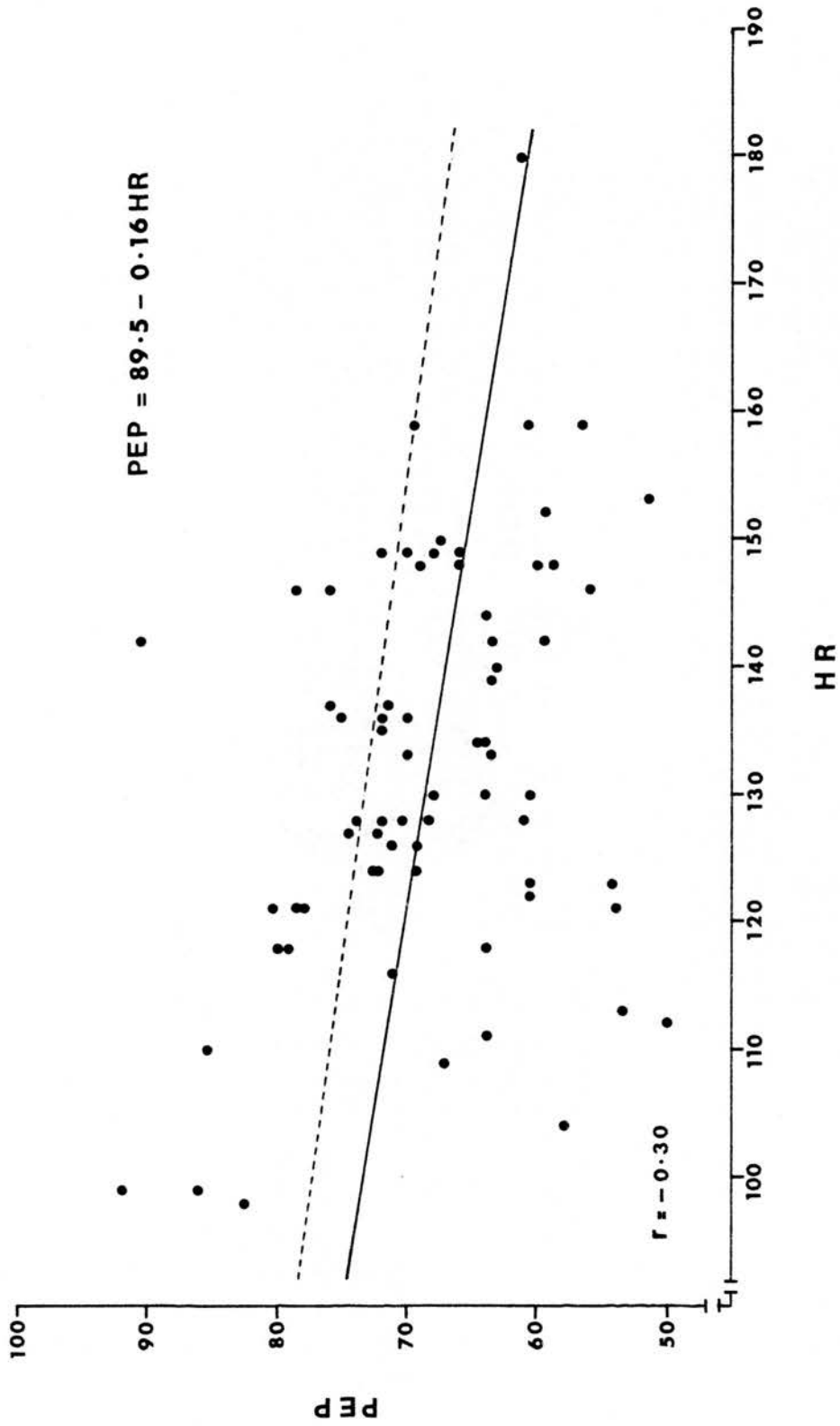
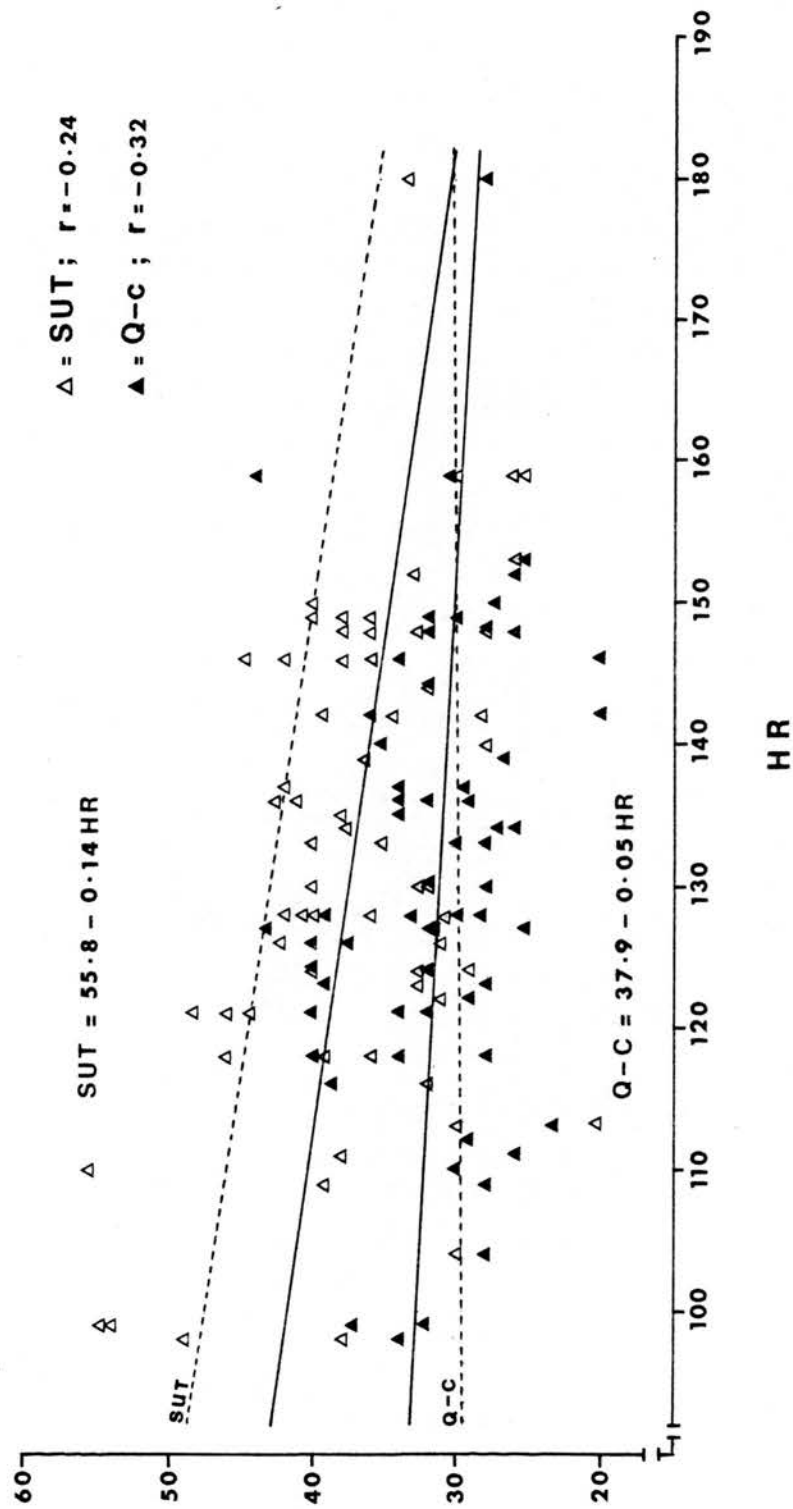


Figure 3.3 (d)



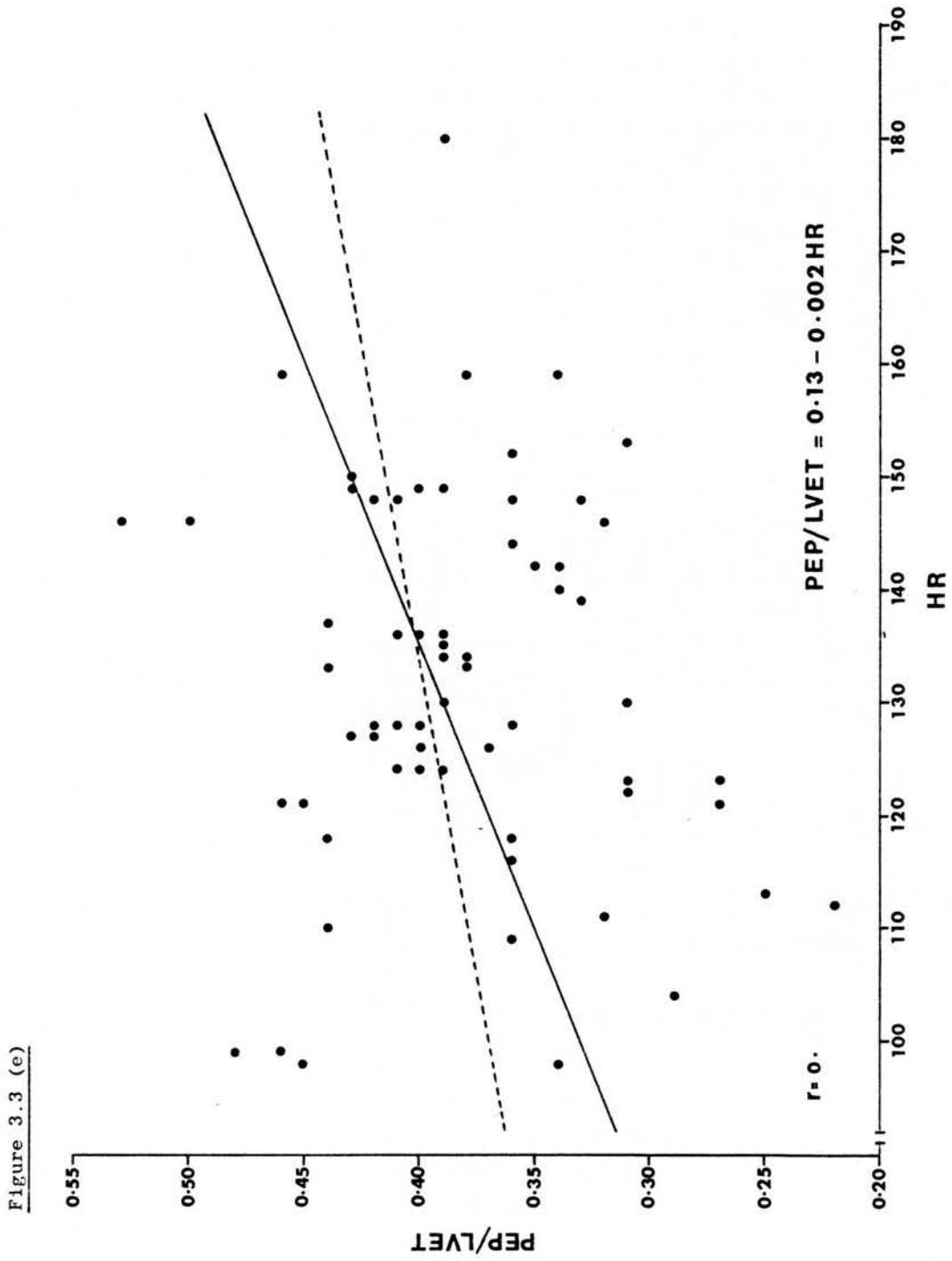


Table 3.5 : STI from Group C Dogs (after coronary artery ligation)

	<u>S.D.</u>	<u>Correlation</u>	
QS ₂ = 354.3 - 0.82 HR	15.85	-0.84	P<0.001
LVET = 266.1 - 0.67 HR	15.19	-0.70	P<0.001
PEP = 89.5 - 0.16 HR	8.80	-0.30	P<0.01
Q-C = 37.9 - 0.05 HR	4.94	-0.16	N.S.
SUT = 55.8 - 0.14 HR	7.04	-0.32	P<0.01
PEP/ = 0.39+ 0.002 HR	0.06	0.09	N.S.
LVET			

Table 3.6 : Comparison of STI : Normal regression data (Group A)
compared with Group C

<u>Group A</u>	<u>Group C</u>	
QS ₂ = 368.7 - 0.83 HR	= 354.3 - 0.82 HR	N.S
LVET = 278.4 - 0.70 HR	= 266.1 - 0.67 HR	N.S
PEP = 90.3 - 0.13 HR	= 89.5 - 0.13 HR	N.S
PEP/ = 0.28+ 0.0009 HR	= 0.39+ 0.0002 HR	N.S
LVET		

Figures 3.4 - 3.6 : Composite Diagram of QS_2 , LVET and PEP vs HR

The durations of QS_2 , LVET and PEP plotted against HR. Each dot represents one measurement (the average taken over five consecutive heart beats). At least one measurement is represented from each dog.

Figure 3.4 : Group A

Figure 3.5 : Group C

Figure 3.6 : Group B

Figure 3.4 : Group A

= QS_2 , $r = -0.90$

= LVET, $r = -0.85$

= PEP, $r = -0.39$

Figure 3.4

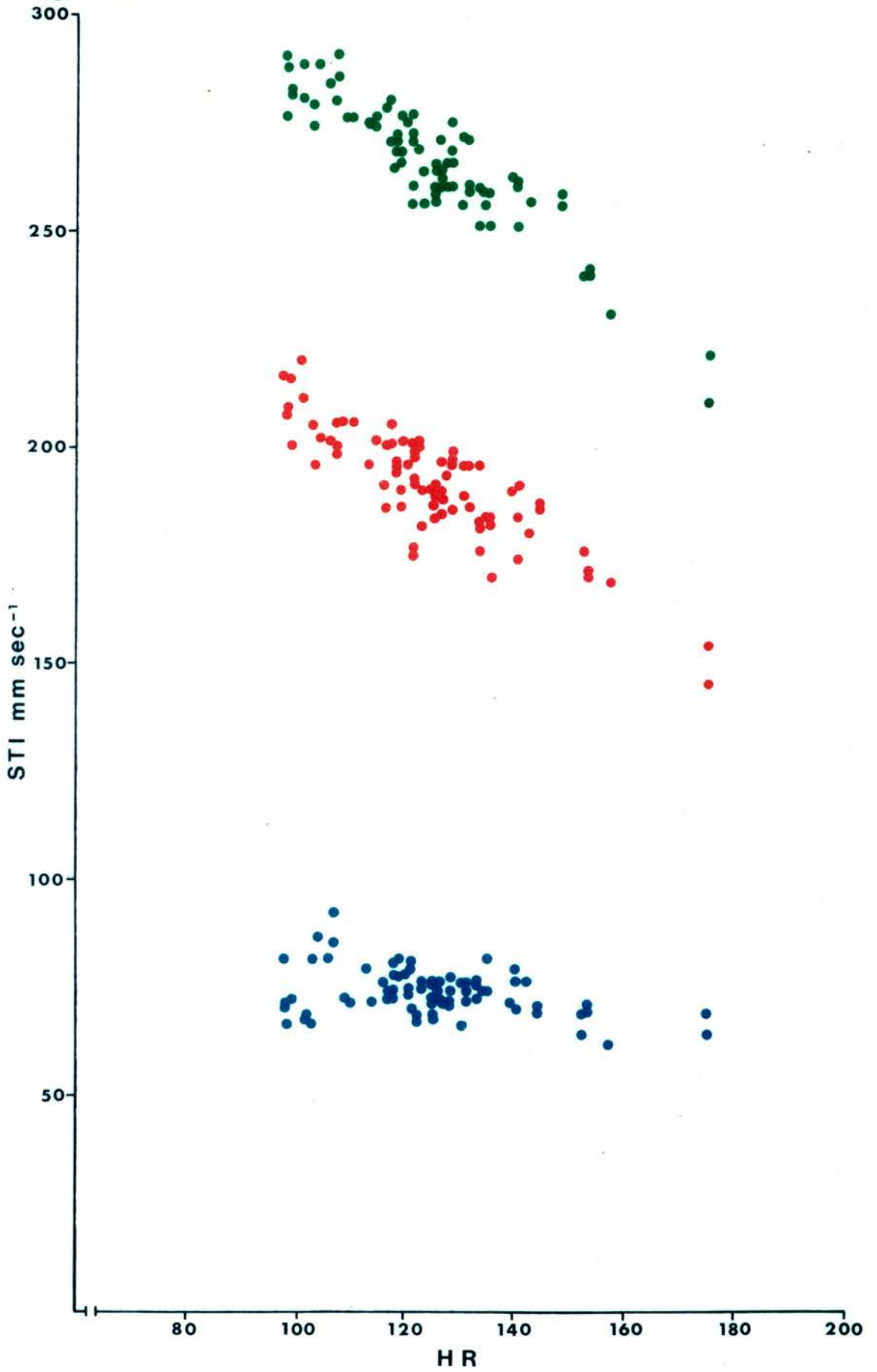


Figure 3.5 : Group C

$$= QS_2, \quad r = -0.84$$

$$= LVET, \quad r = -0.70$$

$$= PEP, \quad r = -0.30$$

Figure 3.5

-97-

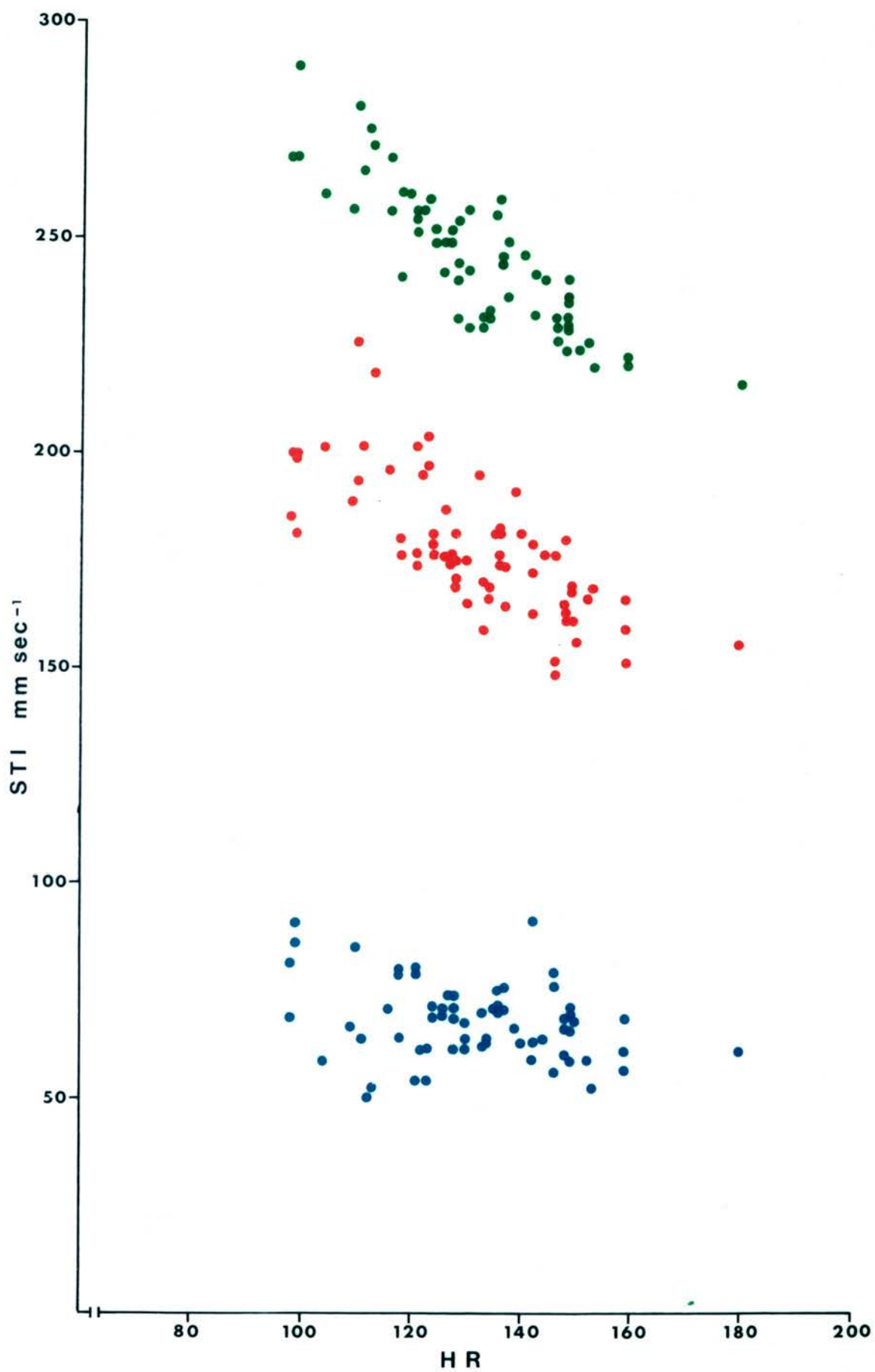


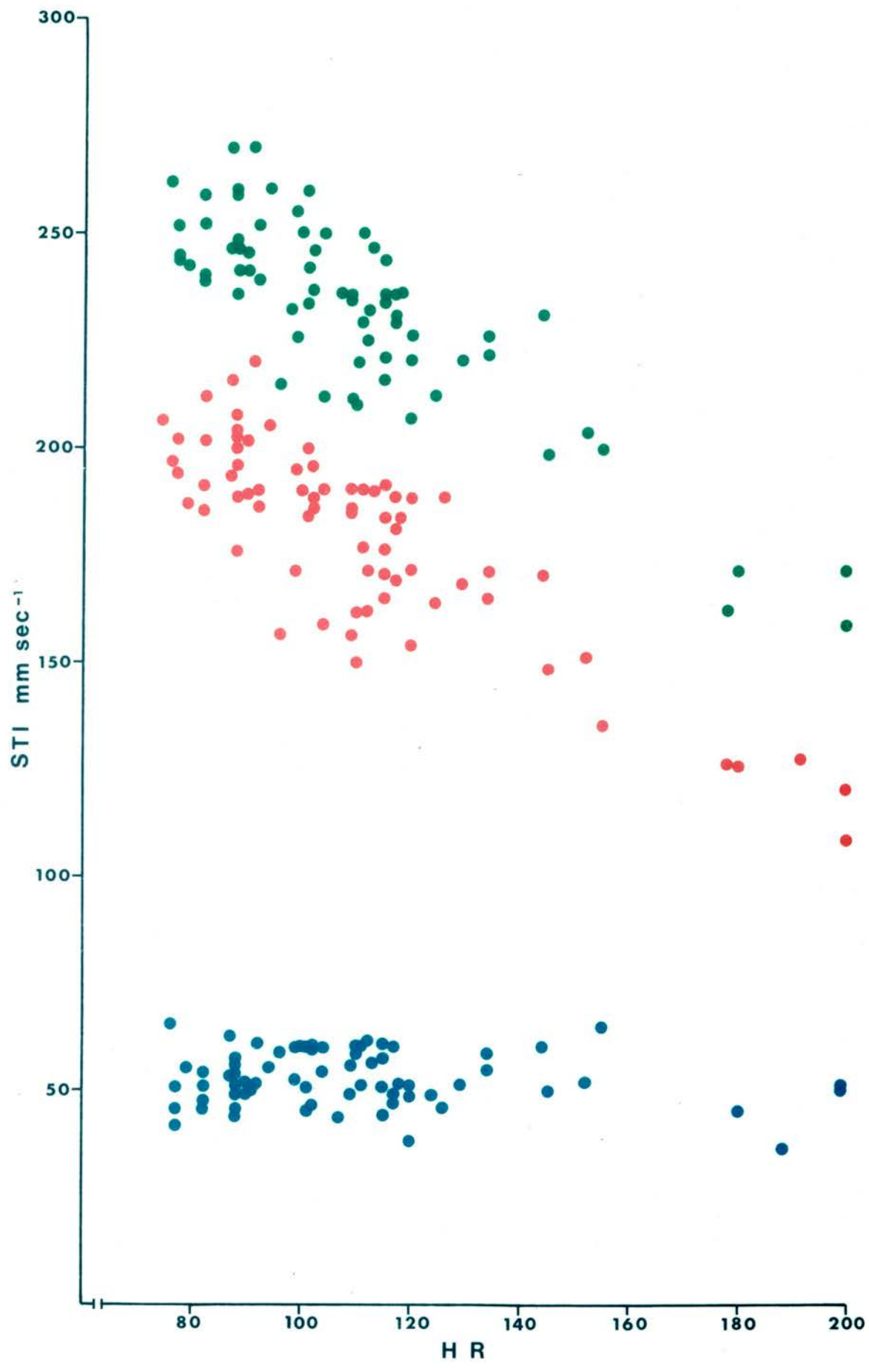
Figure 3.6 : Group B - Conscious Dogs

= QS_2 , $r = -0.88$

= LVET, $r = -0.87$

= PEP, $r = -0.14$ (not significant)

Figure 3.6



3.4 Discussion

This study would only be complete if all the variables which affect the cardiovascular system were known. Full measurements of cardiovascular function might encompass the characteristics of structure (volume, length and area), and velocity and force of contraction. Many parameters such as blood pressure, ventricular volume, myocardial velocity, pre-load, afterload and end-diastolic volume are not readily accessible to measuring devices, without using invasive techniques which are not suitable for use in conscious dogs. For this reason, non-invasive investigations have been employed in this study. However, a major drawback of the technique described here is the inability to define precisely the haemodynamic variables mentioned above which may have a radical effect on the STI.

In this Section, STI were derived from the heart rate, electrocardiogram, apexcardiogram and phonocardiogram. The temporal relationship between the ACG and electrical acoustic and mechanical events has been established in humans (Tafur, Cohen and Levine, 1964) and the ACG has been proved to relate closely to left ventricular pressure events in dogs (Gay et al, 1978). The use of the ACG in man and animals has declined because newer techniques (see General Discussion and Projected Studies) have superseded it. However, the ACG has been used for measurement of STI (Oreshkov, 1965; Spodick and Kumar, 1968; Gabor, Porubszky and Kalman, 1972) and the equipment for ACG recording is readily available to veterinary cardiologists. The difficulties and limitations of the technique are discussed below.

3.4.1 Recording Equipment

For worthwhile apexcardiography, good quality equipment is essential.

This is equally as important for ECG and PCG recording if all three are to be correlated to provide systolic time intervals.

The Siemens - Elema system used was specifically designed for ECG, ACG and PCG recording and provided a high degree of accuracy and resolution. (for technical data see Appendix 1)

Preamplifier

The vibrational energy imparted to the precordium by cardiac activity is present in a wide range of frequencies, some of which lie within audible sound range. However most of the cardiac vibrational energy is contained in sub-audible frequencies. (Johnson and Overy, 1951). A preamplifier should be selected to include the range of all the levels of input amplitude and frequency over which the device is expected to operate. The pulse amplifier, used in conjunction with the transducer, has to be able to cope with low frequency signals from a high impedance source when recording an apexcardiogram.

Transducer

The transducer used in the present study was an air-coupled piezo-electric crystal type. While there is minimal transmission time from the dog to the transducer, there is a possibility of air leaks in this type of transducer. The transducer records the apical movement after its transmission through the pericardium, its fluid contents and muscle, fat and bone, which all affect the passage of low frequency waves. The variables imposed by these intervening tissues make absolute criteria for apexcardiogram amplitude difficult to establish. (Kastor et al, 1970) The size of the pick-up head is important. In these experiments the transducer was 2 cms in diameter, which was considered appropriate for the following reasons:

- a) the transducer was small enough to be accommodated between the dogs' ribs, reducing the attenuation of the signal caused by intervening bone.
- b) the area covered was sufficiently small to allow recording to be restricted to the precise area of the maximal apical impulse.
- c) The small size of the transducer meant that it could be closely applied to the thorax thus minimizing the risks of air leaks (loss of air seal at rim). These have the effect of shortening the time constant thus differentiating (and distorting) the waveform (Mashimo et al, 1966).
- d) A smaller pick-up becomes difficult to hold comfortably.

Although the timing of events may not be changed by the size of the pick-up the contours of the ACG can be altered, and important landmarks obscured (Dimond, Duenas and Benchimol, 1966).

The time constant of the system relates to the ability of a circuit to transmit a long duration pulse of low frequency. A short time constant circuit may be considered as a differentiating circuit which accentuates the rapidly changing segments of a pulse wave (Kastor et al, 1970). This causes distortion of the systolic phases of the ACG in particular and can lead to temporal alterations in the principal landmarks due to unavoidable phase shifts. A time constant of 3 secs is reported to be most satisfactory (Kastor et al, 1970; Johnson, Siegel and Blomquist, 1971; Craige, 1975). The system used in these studies allowed the selection of one of four time constants (0.3 - 7 secs). Four seconds was chosen because it was closest to the pre-selected time constant of the equipment used in Section Four.

Final Amplifiers

The final amplifiers of the Mingo-graph 82 system have a linearity

better than three per cent. The ink-jet galvanometers allow a fast response resulting in no appreciable time lag or hysteresis. These factors allowed precise recording of temporal events of the cardiac cycle. To maintain the accuracy necessary for correct measurement of the STI the ink jets were zeroed before each recording and adjusted to their finest spray.

3.4.2 The Use of Anaesthesia

The most significant problem encountered in the experiments on conscious dogs was the production of artifacts in the ACG. A major source of artifact was movement of the dog (including respiration). The ACG is particularly sensitive since the transducer's function is to sense motion. Mostly the variations produced in the traces by random movement were sufficiently prominent to allow detection. However, subtle variations in waveform, indistinguishable from the measured variable, may have resulted in some inaccuracies in measurement. To minimize these discrepancies, anaesthesia was used while the set of normal STI values (Table 3.1) was being established.

Pentobarbitone sodium was used because of the ease of administration, immediate onset and rapid stability and the long duration of anaesthesia. As a barbiturate, it is not free from cardiovascular effects but the haemodynamic alterations have been considered to be minimal. A paper by Parker and Adams (1978) summarises the following points:

a) In previously unanaesthetised animals the response to a dose of pentobarbitone may include tachycardia and a decrease in systolic and mean blood pressures, stroke volume, pulse and central venous pressure. Tachycardia results from reduced vagal inhibition caused by the drug. The arterial baroreceptor reflex makes an important contribution to the mediation of this effect.

b) Steady state anaesthesia is characterised by an increase in peripheral vascular resistance and a decrease in cardiac output. Premedication can alter this response.

c) Some studies indicate that myocardial contractility can be depressed during anaesthesia. This is probably a direct effect on the muscle, independent of heart rate, preload and other haemodynamic variables.

Pentobarbitone has a direct negative inotropic effect by depressing lipid facilitated membrane calcium ion transport.

X/3.4.3 Limitations of Apexcardiography in Measurement of STI

The most important limitations to the general application of the ACG to dogs is the attenuation of the trace caused by obesity. In conscious dogs, excessive respiratory excursions, especially panting distort the trace (see Fig 2.7). In a few cases, ACGs are not interpretable. The validity of the STI measurements depends upon a clear definition of the onset of QRS, the onset of S_2 , and the beginning and end of ejection. The ACG is used to define the onset of isovolumic contraction and also the point of ejection.

A major criticism of use of the ACG to derive STI is that the E point may not accurately define the onset of ejection. The composite diagrams of ECG, ACG, PCG and CAP which demonstrate the temporal relationship between these measurements and the sequence of cardiac events (Dimond, Duenas and Benchimol, 1966; Gabor, Porubszky and Kalman, 1972) place the E point coincident with the onset of rise of the aortic pulse pressure (see Fig 3.7). The morphological similarity between the left apexcardiogram and left ventricular pressure curves has been recorded (Denef, De Geest and Kesteloot, 1973; Gay et al, 1978) and other papers indicate that the E point clearly delineates the beginning of ventricular ejection (Benchimol, Wu and Dimond, 1966; Tavel et al, 1965; Willems, De Geest and Kesteloot, 1971; Gabor, Porubszky and Kalman, 1972; Gibson, 1975).

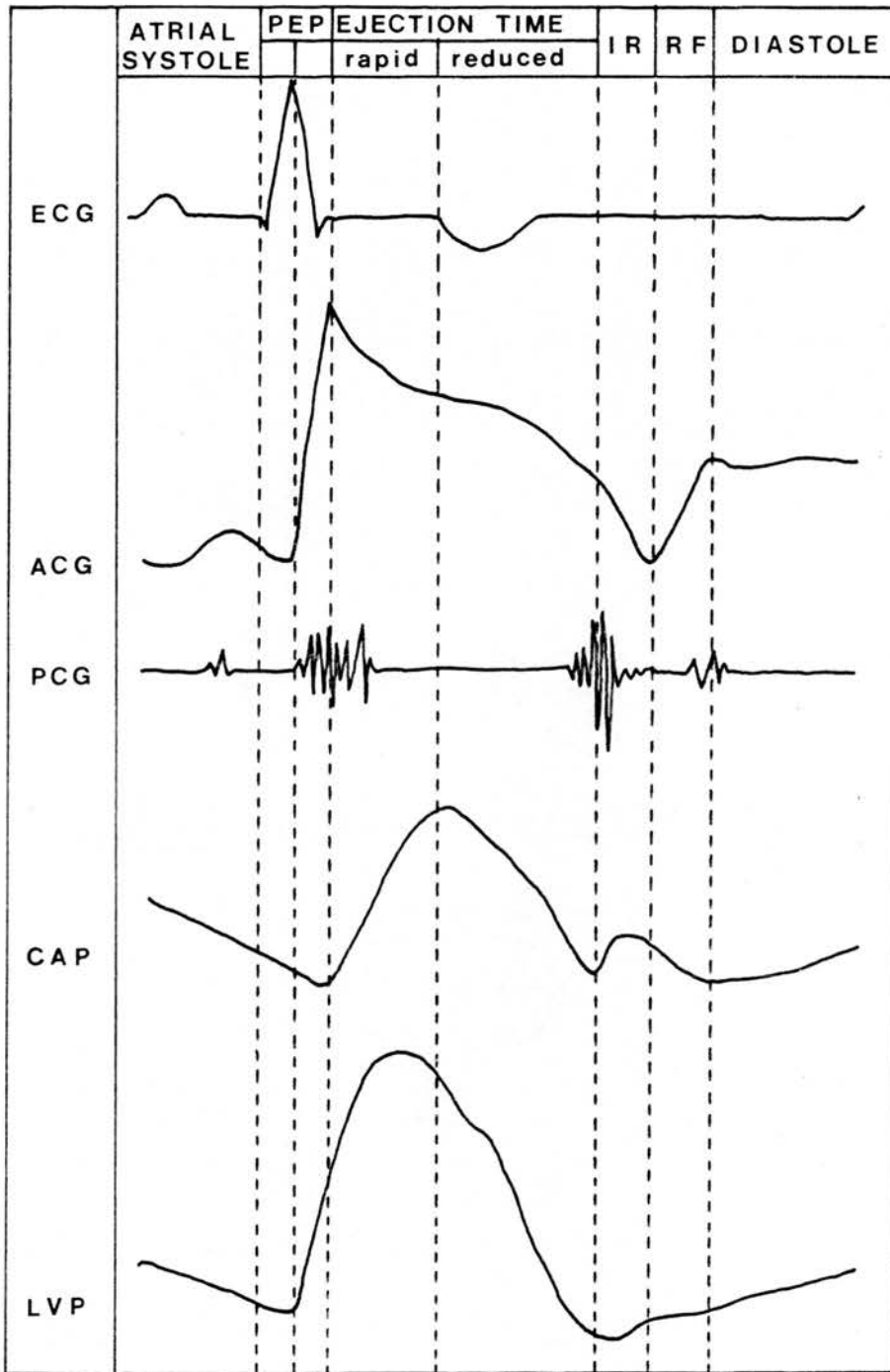


Figure 3.7: Schematic Representation of the Phases of Ventricular Systole showing the correlation between the electrocardiogram, apexcardiogram, phonocardiogram, carotid arterial pulse and left ventricular pressure curve. PEP = pre-ejection period. IR = isovolumic relaxation. RF = rapid filling.

(after Dimond, Duenas & Benchimol, 1966;
Gabor, Porubszky & Kalman, 1972)

However, not all studies support this view (Manolas, Wirz and Rutishauser, 1976; Gay et al, 1978). Because it is not possible to obtain a reliable carotid arterial pulse wave in conscious dogs, no other simple method of indicating the onset of ejection was available for this study. To minimize inaccuracy, only traces which clearly demonstrated a sharp E point were used. The close correlation of the results suggests that even if the E point does not precisely define the point of ejection, there is little variation in the measurements.

The onset of rise of the ACG (C) has been shown to be precisely co-incident with the corresponding event on the intracardiac pressure curve in dogs (Willems, De Geest and Kesteloot, 1971). It is therefore a useful indicator of the start of the isovolumic contraction period. Definition of the C point of the ACG allows the measurement of the sub-intervals of PEP.

Both the C and E points can be identified with precision if careful attention is given to placement of the pulse pick-up, amplification of the transducer signal and to monitoring of the signal on an oscilloscope before recording.

3.4.4 Discussion of Results and Comparison with other Studies

The use of anaesthesia for restraint in normal dogs allowed the collection of data in which landmarks for STI measurement were well defined. Perfect correlation of biological variables is rarely achieved (Swinscow, 1978). Part of the relationship of one variable to another consists of true correlation and part consists of random variation. Thus the strong correlations shown for QS_2 (0.90) and LVET (0.85) indicate not only a relationship between HR and these STI but only a small degree of random variation. Without the use of chemical restraint, less perfect correlations are to be expected.

The results confirm that the STI from anaesthetised and conscious dogs are dissimilar. A healthy, resting dog normally has a heart rate varying between 45 and 120 beats / minute (Hamlin et al, 1967). Normal dogs, anaesthetised and conscious in this study, had heart rates ranging from 60-190 beats / minute. The average heart rate between the two groups did not differ greatly, the anaesthetised rate (114.63) being slightly higher than the conscious value (110.79). The reverse might have been expected, considering the excitability of a conscious dog in strange surroundings, but the higher heart rate in anaesthetised dogs is probably partly stimulated by pentobarbitone sodium (Parker and Adams, 1978). Furthermore, the dogs in this part of the study were accustomed to the recording room; but clinical cases are not similarly acclimatised. Muir and Hamlin (1973) indicate that increased heart rates alter the duration of phases of systole. The heart rate - dependent STI (QS_2 and LVET) are likely to show such variation. Although it can not be assumed that any alteration of systole is due to a heart rate response alone, regression equations may be used to derive the STI, independent of heart rate.

The regression lines of QS_2 , LVET, PEP and the PEP/LVET all showed significant differences between anaesthetised and conscious values. Pipers et al (1978) established STI values for anaesthetised and conscious dogs. Although the technique used was not apexcardiography, it forms a useful comparison for this study, since the heart rate range is similar. The same relationship between anaesthetised and conscious values was noticed for QS_2 , LVET and PEP/LVET but in their study PEP was not significantly altered by anaesthesia.

The anaesthetised values for LVET were generally higher, than the conscious values (190.81 msecs compared with 179.12 msecs). Ejection time is altered by changes in stroke volume, ventricular contractility and possibly by changes in arterial ejection pressure.

If, during steady state anaesthesia, there is an increased arterial pressure, then this may prolong the LVET according to Wallace et al (1963). However, Weissler et al (1969) believe the opposite to be true. No single factor will account for a variation in STI and although arterial pressure may alter the LVET, it is more likely that primarily alterations in ventricular performance are dominant. One known effect of pentobarbitone sodium is direct depression of the myocardium, by affecting membrane calcium ion transport (Parker and Adams 1978).

The duration of QS_2 is derived from the summation of PEP and LVET, and was therefore longer after anaesthesia. PEP, although less dependent on heart rate, was significantly ($p < 0.001$) longer in anaesthetised dogs. In man, PEP has been correlated with contractility of the heart and it is known to vary directly with changes in preload, heart rate and left ventricular end-diastolic pressure. In dogs, PEP is less dependent on heart rate but it may be affected by preload and aortic pressure (Talley, Meyer and McNay, 1971), both of which were unknown quantities in this study. Transient increases in afterload lengthen the PEP and this may be the effect of steady-state anaesthesia. The possible depression of the myocardium, mentioned in the above paragraph, may contribute to a decreased (LV dp/dt) and account for a prolonged PEP.

The PEP/LVET was greater in anaesthetised dogs, although the difference was not so marked ($p < 0.01$). Diminished left ventricular performance will result in an increase in PEP/LVET (Weissler, Harris and Schoenfeld, 1969) and therefore the same factors may be responsible for this increase during anaesthesia .

The comparison between STI from anaesthetised and conscious dogs was performed in the same 18 dogs, whereas Piper et al (1978) used different dogs for each assessment. Use of the same dogs was likely to give less biological variation between the two states.

It is interesting to note that there was difference between the group of 30 normal anaesthetised dogs providing the regression data in Table 3.1 and the group of 18 dogs selected for conscious experiments. This is perhaps explained by the smaller group size. Between the two samples there is likely to be a chance variation which is partly dependent on the amount of variation in the population from which they are drawn. It is a common observation that a small sample is a much less certain guide to the population from which it was drawn than a large sample. A consequence of this is that if two samples are drawn from a population, the larger they are the more closely are they likely to resemble each other (Swinscow, 1978).

3.4.5 Effect of Myocardial Ischaemia on STI

In the comparison of STI from normal dogs with those taken after coronary artery ligation, no significant differences were found between the values for QS_2 , LVET, PEP and PEP/LVET after three months. (Table 3.6)

The development of myocardial ischaemia may be divided into two phases: the initial five days during which critical changes in the STI occur, and a later period in which the STI slowly return to normal. According to published data on myocardial infarction in man and experimental dogs, a shorter PEP and SUT is expected during the initial forty-eight hours, as the sympathetic activity is increased, following the insult to the myocardium (Jain and Lindahl, 1971). Analysis of ACGs in acute myocardial ischaemia (Waagstein, Hjalmarson and Wasir, 1974) demonstrated reduced PEP, IVCT and LVET and a higher A/H ratio (see Section 1.4). This occurred in conjunction with increased systolic blood pressure, which indicated depressed ventricular function compensated by a higher ventricular filling pressure and tachycardia.

Concomitant congestive heart failure may cause an increase in the PEP (Weissler, Harris and Schoenfeld, 1969). The LVET may be unchanged (Lewis et al, 1977) during this period of adrenergic activity and coupled with the concurrent shortening of PEP may give rise to a low PEP/LVET. Therefore a "normal" PEP/LVET may conceal ventricular dysfunction while there is increased sympathetic activity.

In this study, it was not possible to record the ACG during the initial phase of myocardial ischaemia because the thoracotomy wound interfered with placement of the transducer on the chest wall. However recordings taken three months after coronary artery ligation showed reduced values for QS_2 , LVET, PEP, Q-C and SUT, although the differences were not statistically significant. During this three month period, none of the dogs exhibited any clinical signs of heart failure despite quite marked ischaemia of the myocardium at post mortem examination (Alps et al, 1983). The left ventricular end-diastolic pressure had been recorded as normal at the time of the second recording. It must be concluded that the STI failed to indicate the underlying cardiac dysfunction in these cases. It has been noted that in man the STI are abnormal in clinically ill patients (Lewis et al, 1974), but that they will not predict haemodynamic abnormalities which are not clinically obvious.

SECTION FOUR

SYSTOLIC TIME INTERVALS FROM THE APEXCARDIOGRAM

IN DOGS WITH HEART DISEASE

4.1 Introduction

In the previous two sections, the use of the ACG in the dog has been assessed. In Section Two a qualitative appraisal of the ACG indicated that the ACG was easily obtained in most dogs. The measurement of STI from simultaneous recordings of the ECG, ACG and PCG allowed quantitative information to be graphically demonstrated (Section Three). The good correlation between the results presented in Section Three and published data on human STI prompted a further investigation into the use of STI in clinical cases.

A number of authors have published details of STI in dogs. Because of the difficulty in obtaining an external carotid pulse in dogs, in many projects an invasive technique has been used (Wallace et al, 1963; Tally, Meyer and McNay, 1971). The use of the ACG as a non-invasive method for timing intra-cardiac events in dogs with heart disease has been limited (Gay et al, 1978). This is mainly because the use of echocardiography has allowed accurate external measurement of the cardiac function (Pipers, Andrysko and Hamlin, 1978; Boon, Wingfield and Miller, 1983; Lombard, 1984) without the problems inherent in ACG analysis.

Since the cost of echocardiography equipment is outwith the budget of many veterinary clinics, the ACG is potentially valuable in deriving STI in dogs. STI are assessed in this Section in various breeds of dogs with suspected or clinically evident heart disease.

4.2 Materials and Methods

The majority of dogs in this Section were seen as out-patients at the Small Animal Clinic of the Royal (Dick) School of Veterinary Studies. A few were hospitalised within the Veterinary School. These animals were presented with suspected or proven heart disease. Apexcardiograms were recorded in 61 dogs (age range 6 months to 15 years - Table 4.1). ACGs suitable for quantitative measurements were obtained from 38 dogs. Of these dogs, 8 were found, on further investigation, to have no cardiovascular abnormality. The reasons for not obtaining satisfactory recordings in 23 dogs are discussed in Section 4.3.1.

4.2.1 Recording Procedure

A full history was taken. Clinical examination of all referred cases included a general external examination followed by specific cardiac investigation in a routine suggested by Darke (1979). This comprises palpation, percussion, auscultation, radiography, electrocardiography and cardiac catheterisation, if required. The dogs were then removed to a quiet room for ECG, ACG and PCG recordings. The standard limb leads were attached using crocodile clips and saline jelly. Each dog was gently restrained in left lateral recumbency. Every attempt was made to encourage the dog to relax. Recordings took place over several respiratory cycles, with respirations being obstructed if they interfered with the trace. The external nares were blocked while the mouth was held closed. The point of maximal apical impulse was determined and the transducer held against the left thoracic wall. Some animals became distressed in the recumbent position and recordings were taken with the dog in sternal recumbency or standing. No chemical restraint or sedative was used. Recordings took place almost without exceptions between 14.00 - 17.00 hours.

Table 4.1 : Breeds of Dogs in which the ACG was Recorded

This table shows all the breeds of dogs which were presented for ACG recording. ACGs suitable for STI measurement were recorded in 38 dogs out of a total of 61.

Table 4.1

Afghan	1	Pointer	1
Alsation	1	Poodles Toy	2
Border Collie	5	Minature	3
Border Terrier	1	Standard	1
Boxer	5	Rhodesian Ridgeback	1
Bull Terrier	1	St Bernard	3
Chihuahua	1	Samoyed	1
Chow	1	Setter - English	1
Cross-bred	7	Irish	1
Doberman	1	Shetland Collie	1
Great Dane	1	Spaniels - Cavalier	5
Greyhound	2	Cocker	1
Hovawart	1	Springer	1
Irish Wolfhound	1	West Highland White Terrier	1
Labrador	5	Whippet	1
		Yorkshire Terrier	1

All recordings were made on a Nihon-Kohden, 3 channel ECG recorder, type Cardiofax - 5303 with a PCG-pulse amplifier, type AG 531D (Appendix 1) at paper speeds of 100 mm/sec.

4.2.2. Calculation of STI Indices

The analysis of the recordings was identical to the method described in Section 3.2.4. with the exception of measurement of the derivative of the ACG, dA/dt . The STI were measured independantly of the clinical assessment of the dog.

The STI indices were obtained by transposition of the terms of the regression equation and calculated as the sum of the measured interval (STI) and the product of the observed heart rate (HR) and the appropriate regression slope (m).

$$\text{STI Index} = (\pm m \times \text{HR}) + \text{STI}$$

The deviations from normal were calculated as the difference between the calculated and the expected normal value at zero heart rate ie. the Y - intercept of the appropriate regression equation.

Table 4.2 : Details of Referred Cases

The breed, age, sex and reason for referred are shown in the table. The results of clinical assessment of the presence or absence of cardiac failure (see Section 4.2) in each dog is indicated by F/C in column 6.

The STI indices for QS_2 , LVET, PEP and PEP/LVET are shown with the deviation from the expected interval in the subsequent column.

Key: M = Male
F = Female
Age = age of dog in years

Abnormality

MI = Mitral incompetence
CHF = Congestive heart failure
APB = Atrial premature beats
VPB = Ventricular premature beats
LBBB = Left bundle branch block
A/V Block = Atrio-ventricular block
AF = Atrial fibrillation
PS = Pulmonic stenosis
AS = Aortic stenosis
VSD = Ventricular septal defect
NAD = No abnormality detected
Ex Intol = Exercise intolerance
F/C Column = Failure/Compensated

Table 4.2

Dog No.	Breed	Sex	Age	Main Clinical		F/C	QS ₂ I	PEPI	LVETI	PEP/LVET
				Abnormality						
80	Border Collie	M	5	M1		C	297 - 19	58 + 1	240 - 20	0.41 + 0.21
79	Poodle	M	10	M1		F	333 + 18	48 - 8	287 + 27	0.50 + 0.30
78	Pekingese	M	10	M1, VPB		F	303 - 12	62 + 6	246 - 14	0.53 + 0.33
76	Whippet	F	2	M1		F	271 - 45	69 + 13	202 - 58	0.54 + 0.34
72	Chow	M	4	M1		F	351 + 3	60 + 3	294 + 34	0.59 + 0.39
70	STD Poodle	M	11	M1		C	353 + 38	74 + 18	285 + 25	0.61 + 0.41
68	Cross-Bred	M	11	M1		F	300 - 13	69 + 12	233 - 27	0.72 + 0.52
67	Border Collie	F	3	M1, Addisons		C	311 - 5	51 - 5	262 + 2	0.56 + 0.36
65	Cav. K.C. Spaniel	M	7	M1		F	305 - 11	59 + 2	248 - 12	0.60 + 0.40
61	Bull Terrier	F	10	M1		C	314 - 1	55 - 2	262 + 2	0.51 + 0.31
60	Cav. K.C. Spaniel	F	10	M1		F	344 + 28	70 + 14	275 + 15	0.61 + 0.41
59	Cav. K.C. Spaniel	F	8	M1		F	330 + 15	58 + 2	274 + 14	0.81 + 0.61
57	Collie Cross	M	9	M1		F	314 - 2	88 + 32	227 - 33	0.71 + 0.51
52	Labrador	M	12	M1, APB		C	358 + 42	73 + 17	286 + 26	0.58 + 0.38
47	Border Collie	M	16	M1, Acute CHF		F	302 - 14	94 + 38	206 - 54	0.34 + 0.14
45	Poodle	M	10	M1		C	304 - 12	48 - 8	255 - 5	0.50 + 0.30
44	Cav. K.C. Spaniel	F	13	M1		C	305 - 10	51 - 6	253 - 7	0.42 + 0.22
43	Springer Spaniel	M	3	M1, APB, VPB		F	265 - 51	87 + 30	179 - 81	0.69 + 0.49
41	Greyhound	F	3	M1		F	310 - 5	72 + 15	240 - 20	0.66 + 0.46
40	Labrador	F	1	M1		F	310 - 6	75 + 18	237 - 24	0.70 + 0.50

Main Clinical

Dog No.	Breed	Sex	Age	Abnormality	F/C	QS ₂ I	PEPI	LVETI	PEP/LVET
71	Sheltie	M	10	VPB	C	305 - 14	61 + 5	245 - 15	0.41 + 0.21
63	Boxer	M	2	A/V Block, LBBS	F	STI MEASUREMENT NOT POSSIBLE (SEE FIG. 4.5)			
54	Labrador	M	5	APB, VPB	F	329 + 14	74 + 17	257 - 3	0.49 + 0.29
42	St Bernard	F	3	AF	F	290 - 25	83 + 26	196 - 64	0.79 + 0.59
75	Bull Terrier	F	1/2	VSD, PS	F	339 + 23	81 - 25	233 - 27	0.59 + 0.39
66	Border Collie	M	3/4	PS	F	323 + 7	103 + 46	222 - 38	1.02 + 0.82
64	Labrador	M	1/2	PS	C	326 + 7	56 + 1	271 + 11	0.48 + 0.28
53	Afghan	F	1½	AS	F	350 + 35	82 + 25	270 + 10	0.70 + 0.50
51	Cross-Bred	F	1½	PS	C	326 + 11	52 - 5	277 + 17	0.55 + 0.35
49	Boxer	F	1	VSD	C	312 - 4	55 - 2	258 - 2	0.49 + 0.29
77	Hovawart	F	4	Collapse, NAD	-	306 - 9	59 + 3	248 - 12	0.45 + 0.25
74	Border Collie	F	1	Collapse, NAD	-	317 + 3	65 + 9	253 - 7	0.43 + 0.23
73	Lab. Retriever	M	4	Collapse, NAD	-	304 - 12	69 + 13	236 - 23	0.48 + 0.28
69	English Setter	M	5	Ex. Intol, NAD	-	322 + 6	66 + 9	258 - 2	0.53 + 0.33
62	Boxer	M	2	LBBS, Normal	-	322 + 7	77 + 21	255 - 14	0.57 + 0.37
58	Pointer	F	8	Collapse, NAD	-	284 - 31	61 + 5	223 - 36	0.46 + 0.26
56	Greyhound	M	6	Ex. Intol, NAD	-	314 - 2	80 + 23	235 - 25	0.55 + 0.35
50	Irish Setter	M	1	Collapse, NAD	-	318 + 2	66 + 8	253 - 7	0.40 + 0.20

4.3 Results

The ACG, ECG and PCG were recorded in 61 dogs. The recordings were of suitable quality for STI measurement in 38 dogs of various breeds. (Table 4.2)

4.3.1. Reasons for Poor Quality Apexcardiograms

The main reasons for poor quality recordings were:

- (i) Excessive movement of the dog due, for example, to excitement and panting (Fig 4.3) or dyspnoea in cardiac failure;
- (ii) Pan-systolic murmur obliterating the aortic component of the second heart sound (S_2 component of QS_2) (Fig 4.4);
- (iii) Dysrhythmias preventing measurement of RR intervals and sometimes disguising the Q wave of the ECG (Figs 4.5 and 4.6)
- (iv) A pansystolic musical murmur in one dog interfered with ACG frequencies (Fig 4.7).

4.3.2. Systolic Time Intervals

The linear regression equations are shown in Table 4.3.

Table 4.3 : STI in Dogs with Clinical or Suspected Heart Disease

Systolic

Interval	Regression Equation	S.D.	Correlation	
QS ₂	= 277.4 - 0.46 HR	27.23	-0.69	P<0.001
LVET	= 193.1 - 0.31 HR	22.52	-0.56	P<0.001
PEP	= 82.0 - 0.14 HR	13.34	-0.42	P<0.001
Q-C	= 33.6 - 0.06 HR	5.95	-0.40	P<0.001
SUT	= 47.8 - 0.08 HR	9.43	-0.34	P<0.001
PEP/ LVET	= 0.44 - 0.00006 HR	0.13	-0.02	N.S.

All values are expressed in milliseconds.

S.D. = Sample standard deviation

N.S. = Not statistically significant

The equations were derived from 73 measurements which are shown in relation to heart rate in Fig 4.1 (a) - (e). For the purpose of comparison, the regression lines (± 1 SD) for normal, conscious dogs (Table 3.2) are superimposed in Fig 4.1 (a) - (c) and (e).

QS₂ differed significantly (P<0.001) from zero and from normal, demonstrating an overall shortening of the interval. LVET exhibited a clear inverse relationship with HR and was not significantly different from the normal value calculated for LVET. PEP showed a negative correlation of 0.4 which differed significantly from zero. The interval also differed from the normal PEP (P<0.001) showing a marked lengthening in clinical cases, due to an increase in both Q-C and SUT (Fig 4.1 d). The regression for PEP/LVET did not differ from zero but was significantly different (P<0.001) from the normal regression line, the ratio being markedly increased. These comparisons are tabled below.

Figure 4.1 (a) - (e)

STI Obtained from Referred Cases

- a) QS_2
- b) LVET
- c) PEP
- d) Q-C and SUT
- e) PEP/LVET

In all graphs, the regression line is drawn (continuous line) and for comparison, the regression line for normal conscious dogs (Group B) is superimposed (dotted line).

In all graphs, except Fig 4.1 (d), the area representing $\pm 1SD$ of the normal regression line is shown (shaded area).

Figure 4.1 (a)

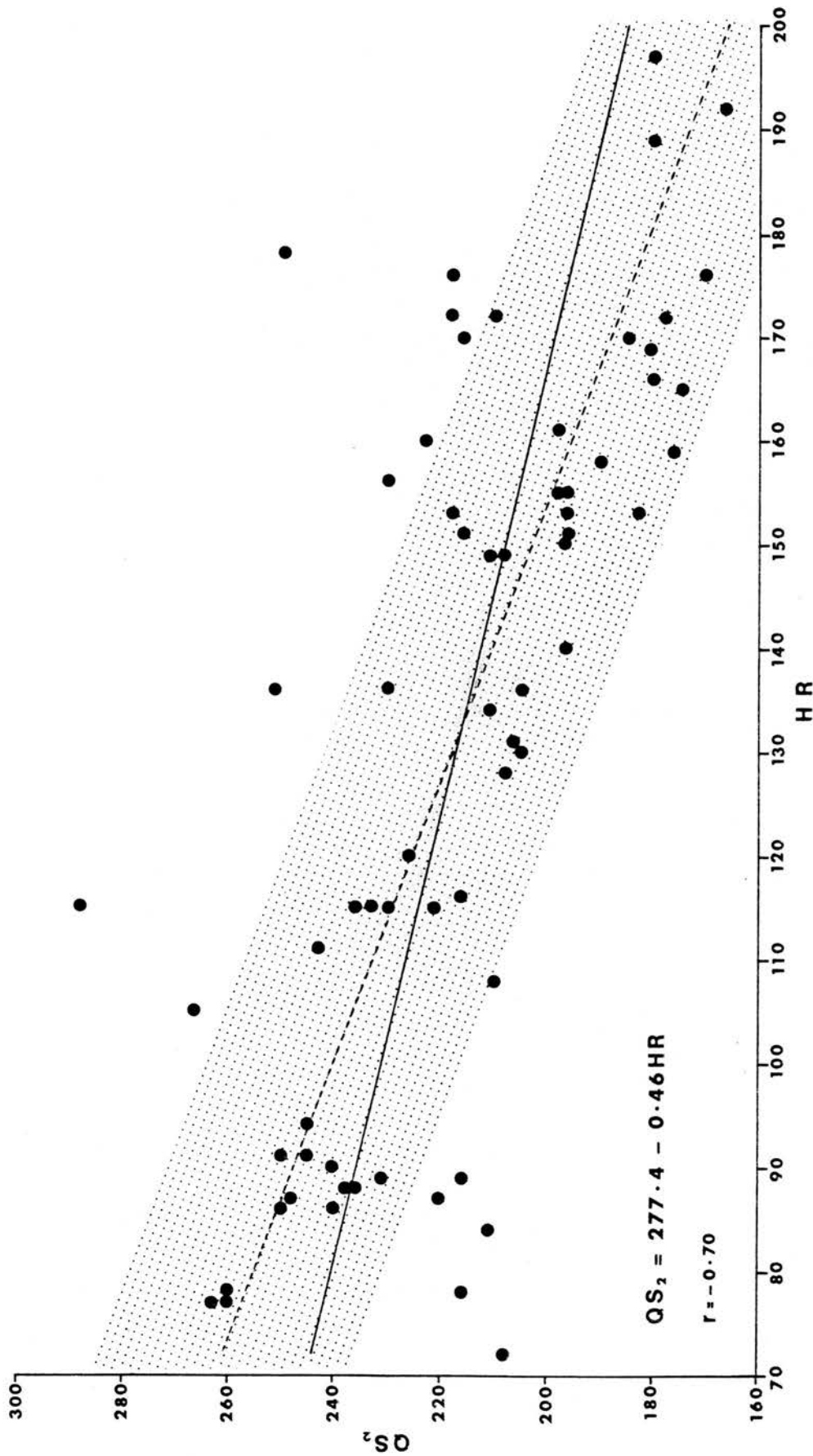


Figure 4.1 (b)

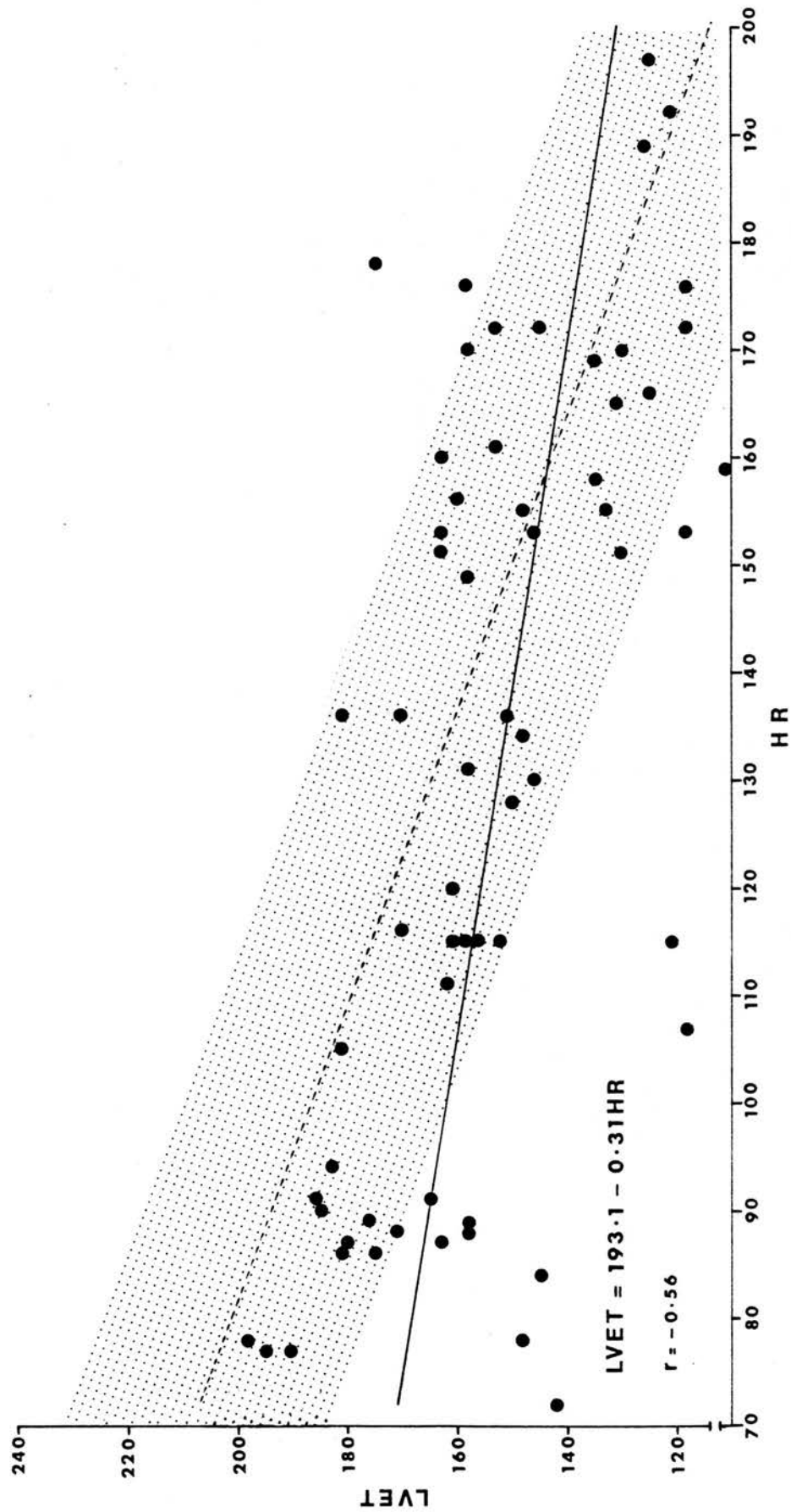


Figure 4.1 (c)

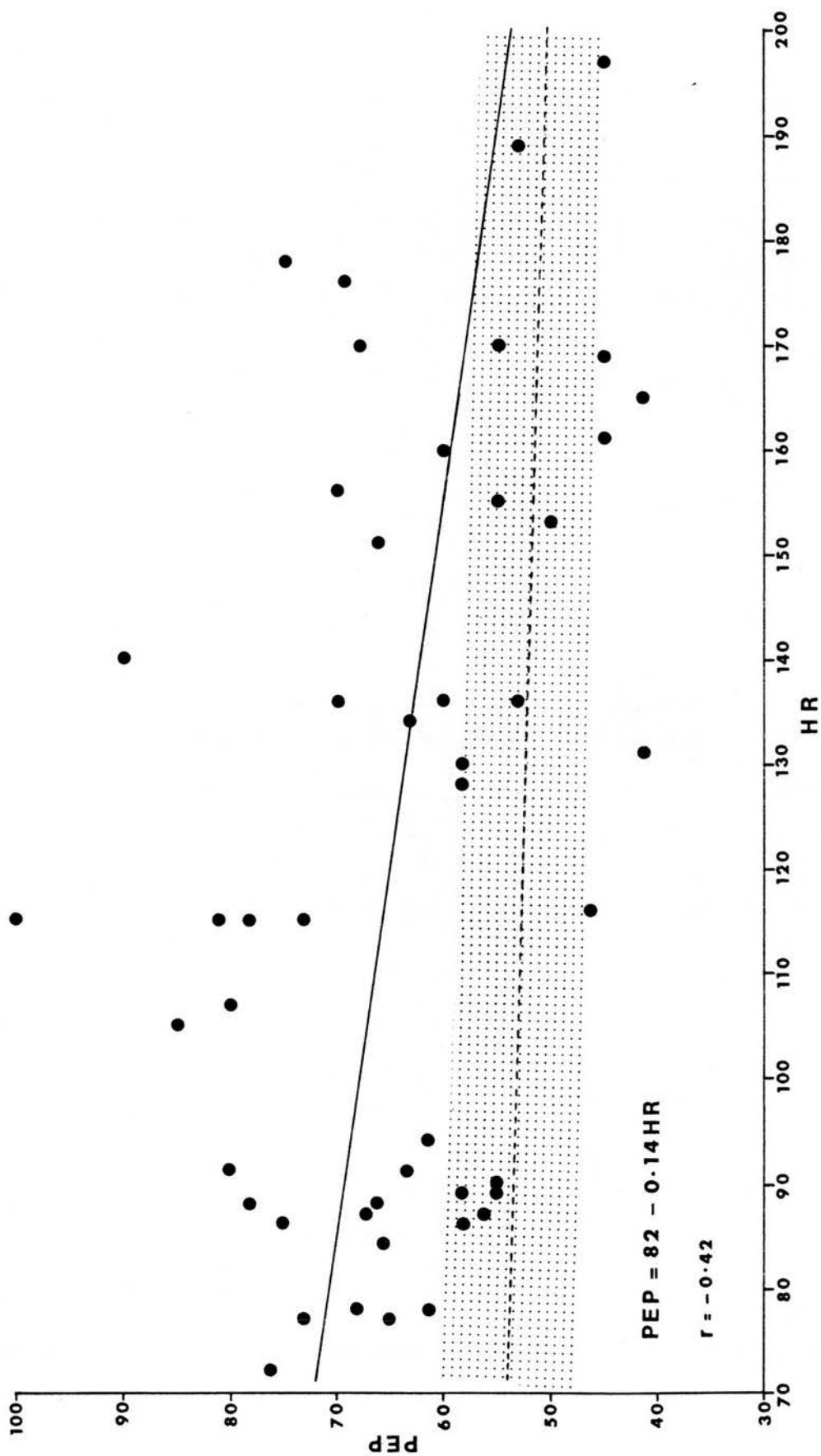


Figure 4.1 (d)

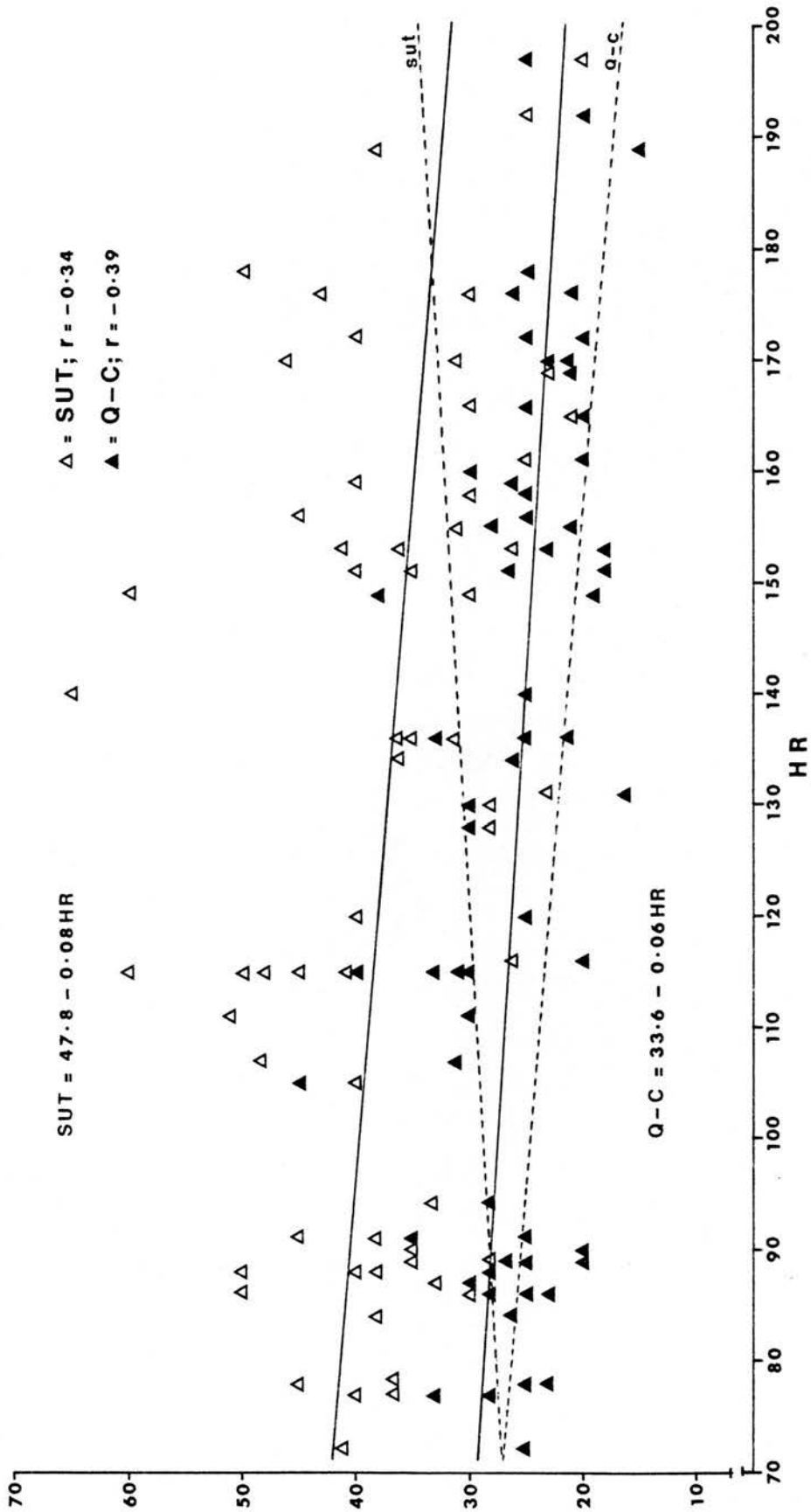


Figure 4.1 (e)

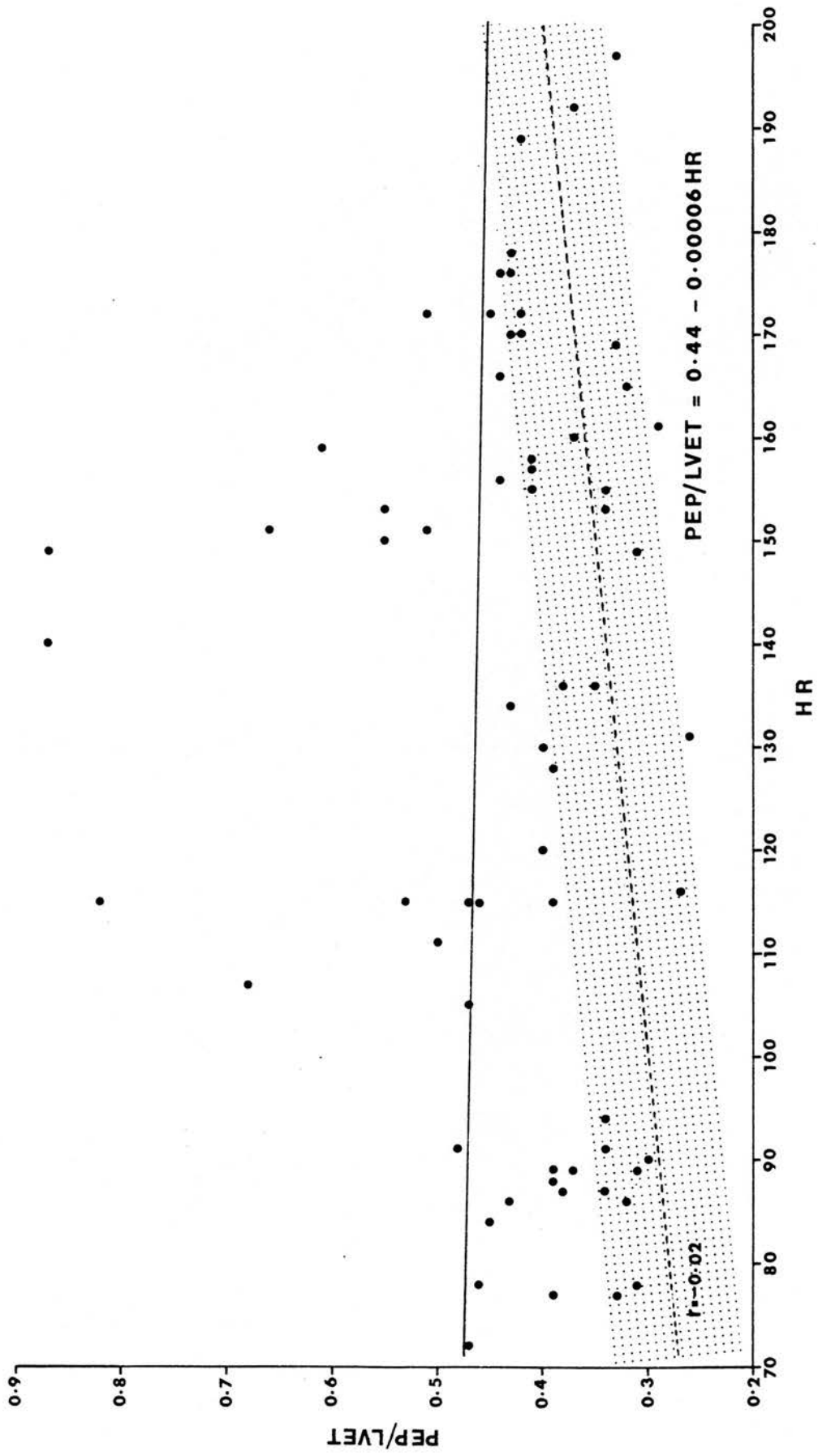


Figure 4.2

Composite Diagram of QS_2 , LVET and PEP vs HR

The durations of QS_2 , LVET and PEP are plotted against HR. Each dot represents one measurement (the average taken over five consecutive heart beats). At least one measurement is represented from each dog.

$$= QS_2, r = -0.69$$

$$= LVET, r = -0.56$$

$$= PEP, r = -0.42$$

Figure 4.2

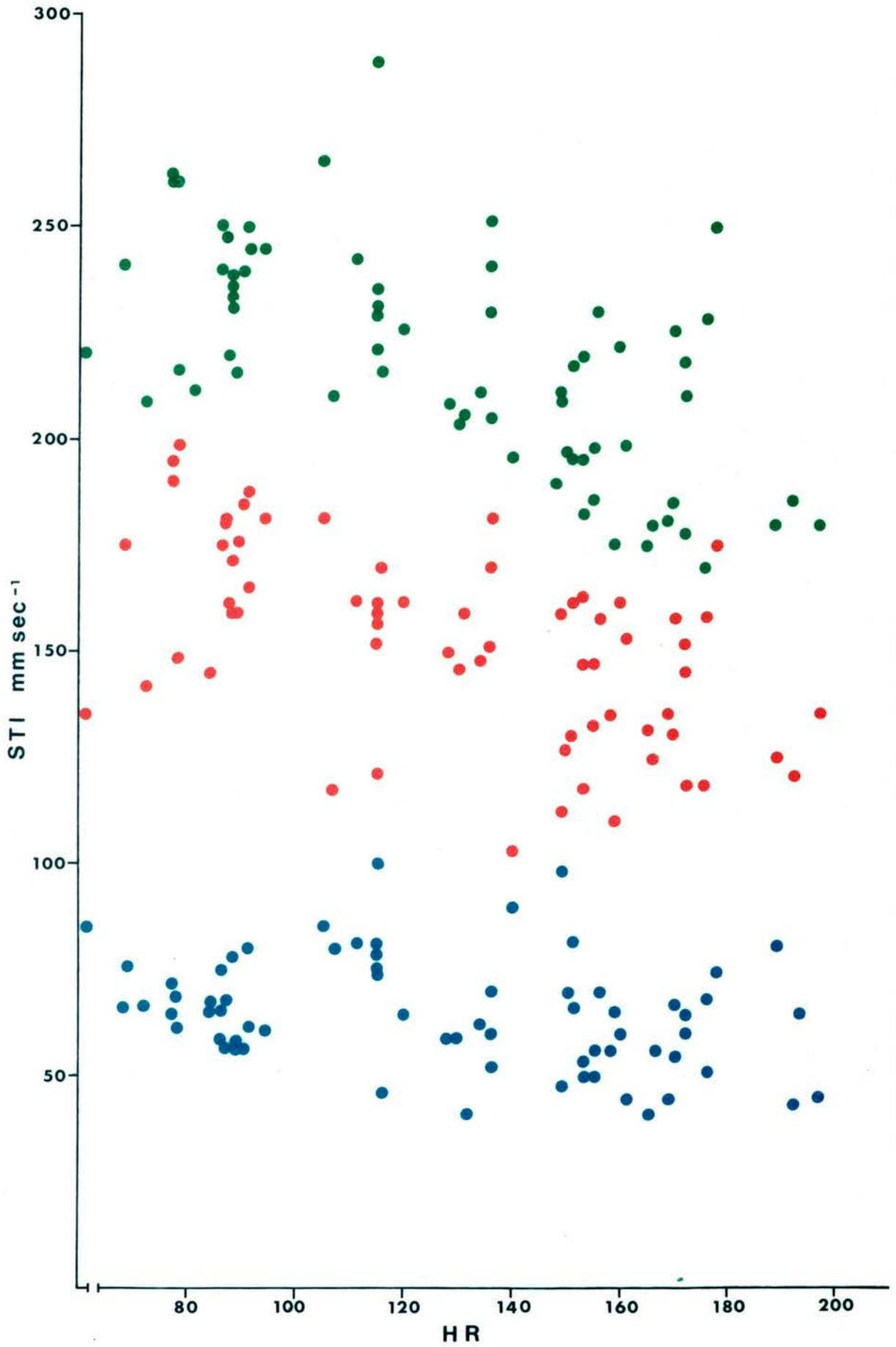


Table 4.4 : Comparison between STI in normal dogs and referred cases

	Normals	Referred Cases		
QS ₂	= 315.5 - 0.75 HR	= 277.4 - 0.46 HR	Signif diff.	P<0.001
LVET	= 260.0 - 0.73 HR	= 193.1 - 0.31 HR	N.S.	
PEP	= 56.4 - 0.03 HR	= 82.0 - 0.14 HR	Signif diff.	P<0.001
PEP/ LVET	= 0.20- 0.001HR	= 0.44- 0.00006HR	Signif diff.	P<0.001

Eight dogs referred for suspected cardiovascular disease were considered to have no apparent cardiovascular abnormality on further examination. The following comparison was made between the STI obtained in 18 normal Beagles (Table 3.2) and the 8 dogs of various breeds (Table 4.2). The two sets of values demonstrated no significant differences for QS₂, LVET, PEP and PEP/LVET (see Table 4.5).

Table 4.5 : Comparison of STI between normal Beagles and normal dogs of various breeds

	Beagles	Various Breeds	
QS ₂	= 315.5 - 0.75 HR	= 295.1 - 0.58 HR	0.10>P>0.05
LVET	= 260.0 - 0.73 HR	= 244.6 - 0.51 HR	0.05>P>0.01
PEP	= 56.4 - 0.03 HR	= 79.8 - 0.17 HR	P>0.50
PEP/ LVET	= 0.20- 0.001HR	= 0.44- 0.002HR	P>0.50

Figure 4.3

The Effect of Panting on the ACG in the Dog

Cross-bred, Female, 9 years old.

The arrow indicates the onset of panting. Note the complete distortion of the ACG and the deterioration of clarity in the PCG.

Figure 4.3

100 mm sec⁻¹

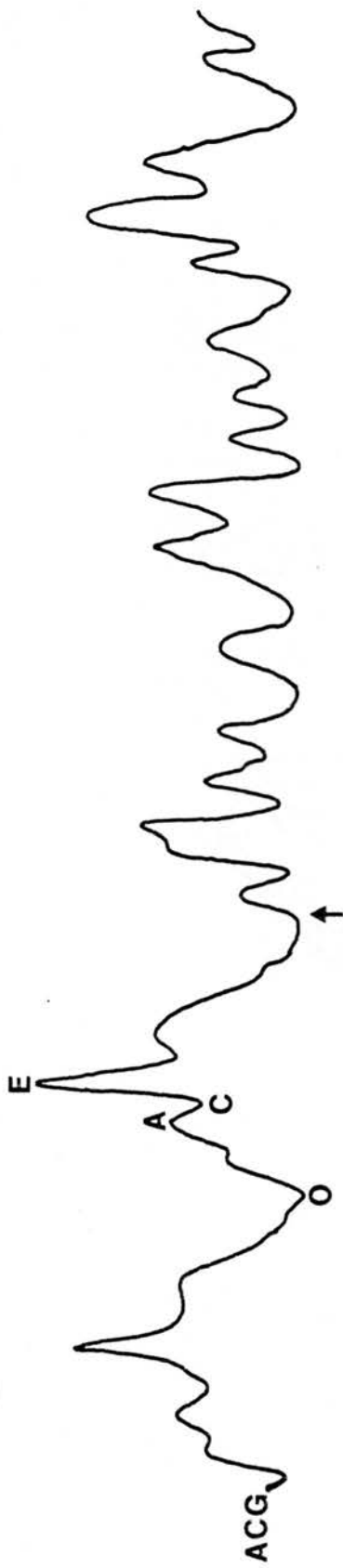


Figure 4.4

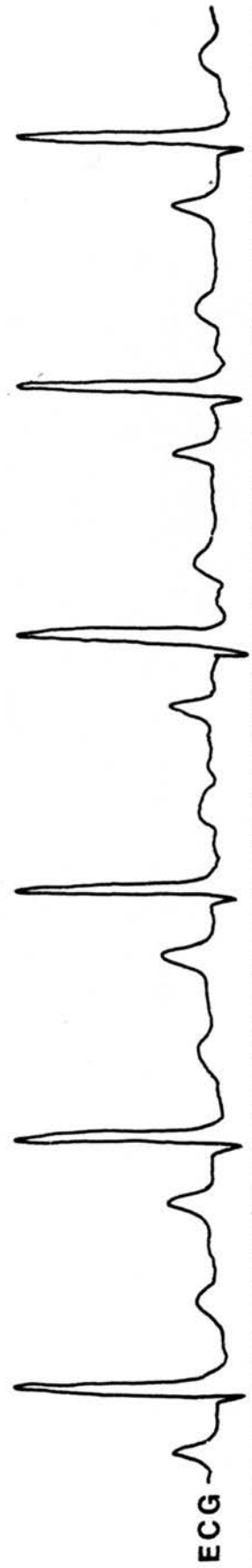
Pan-Systolic Murmur Preventing Measurement of the ACG

Bull Terrier, Female, 10 years old.

Measurement of QS_2 was not possible because the pan-systolic murmur obscured the onset of the second heart sound.

Figure 4.4

100 mm sec⁻¹



Figures 4.5 and 4.6

Distortion of the ACG in Dysrhythmias

Boxer, Male, 2 years old.

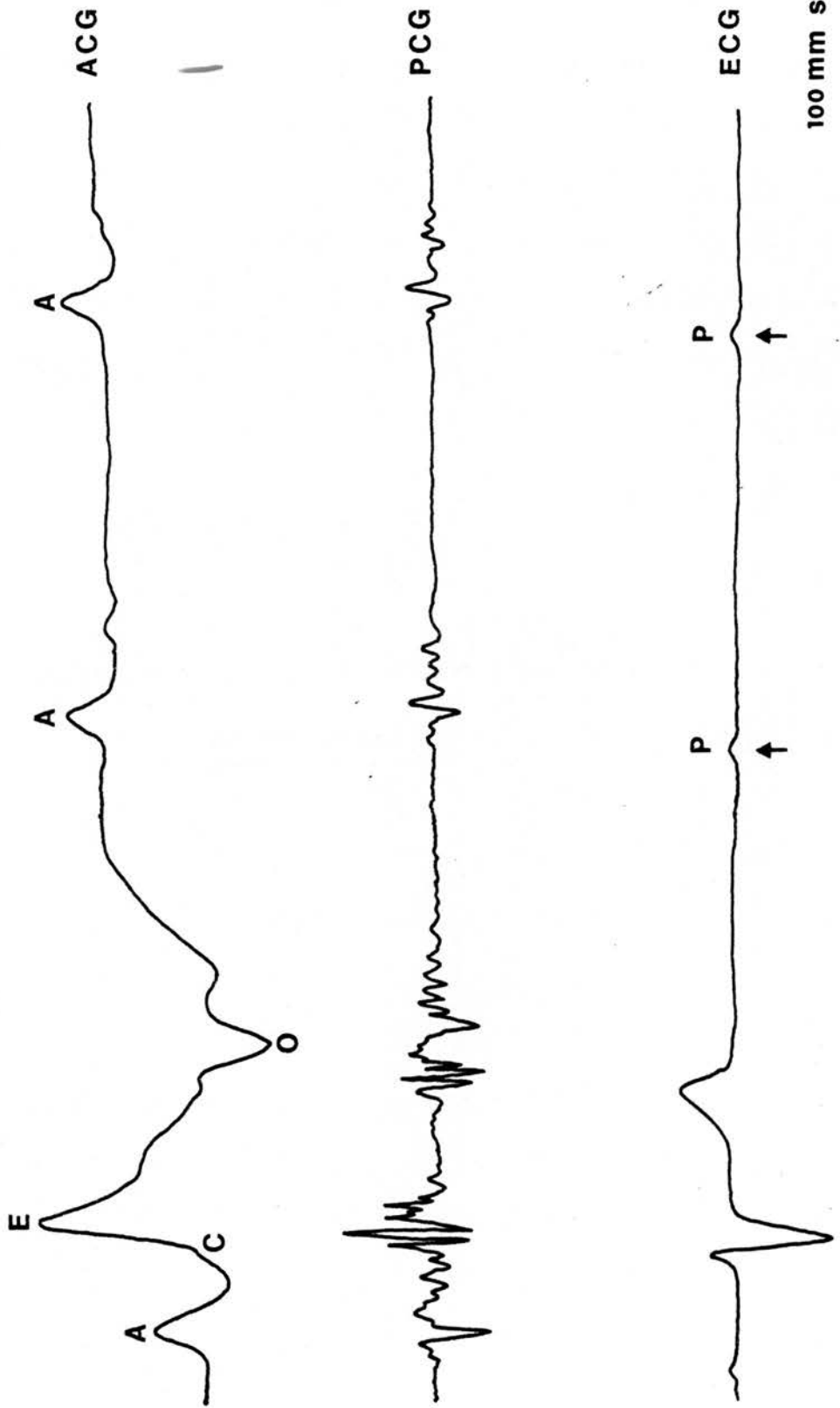
Fig 4.5

February 1981 - total A/V block resulted in intermittent, normal - shaped ACG despite left bundle branch rhythm. RR intervals could not be measured.

Fig 4.6

March 1982 - ectopic beats caused distortion of the ACG and PCG which disallowed measurement of STI from these extrasystoles. Other beats were normal.

Figure 4.5



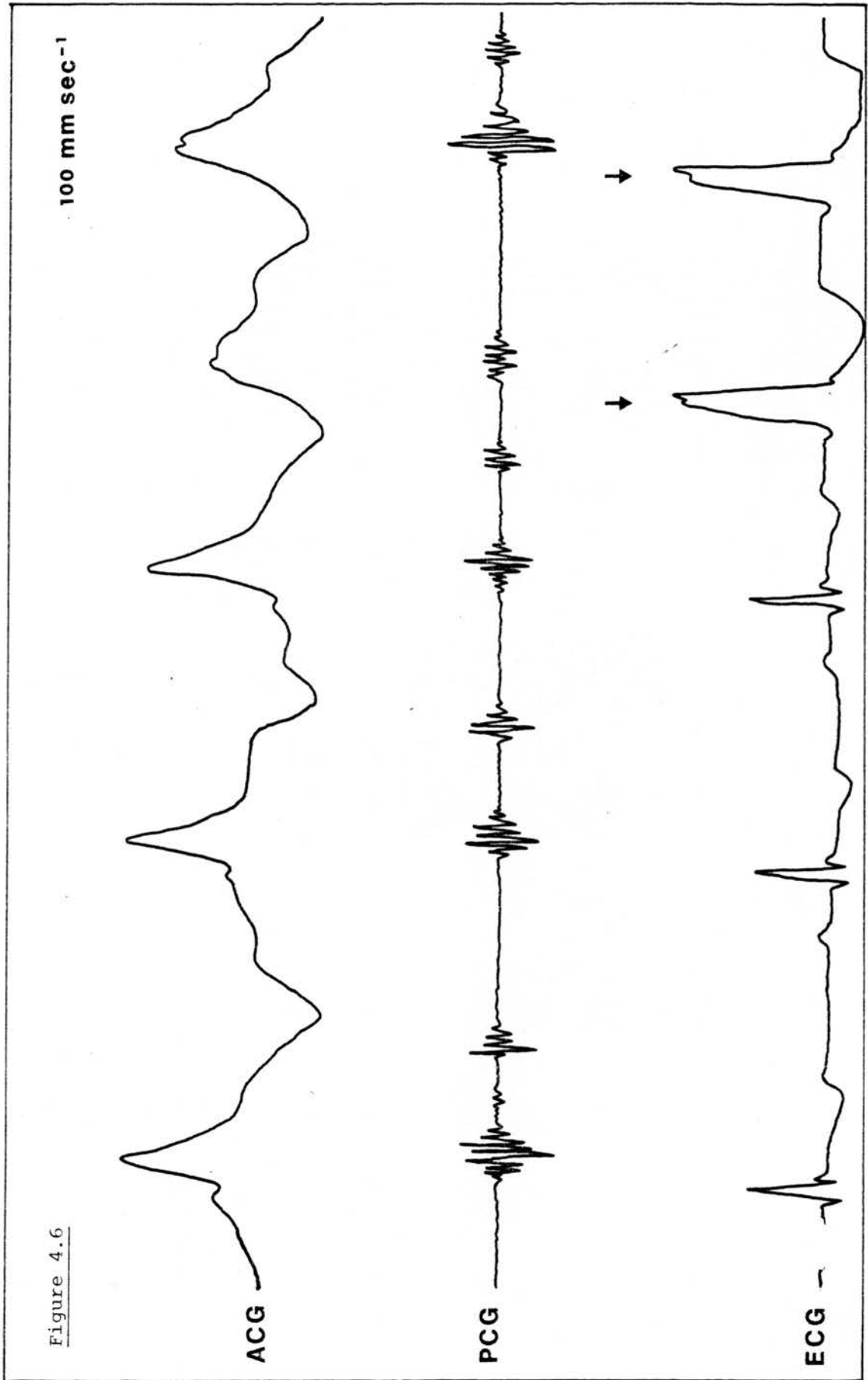


Figure 4.7

Interference with ACG Frequencies

Cavalier King Charles Spaniel, Female, 8 years old.

An unusual pan-systolic musical murmur caused distortion of the PCG. The vibrations occurring during ejection are reflected on the downstroke of the ACG.

Figure 4.7



100 mm sec⁻¹

4.3.3. Systolic Time Intervals Indices

The STI indices are shown in Table 4.2. The deviations from normal are indicated by the signed values (+ or -). These deviations are shown graphically in Fig. 4.8 (a) - (c).

Fig 4.8 (a) presents a wide scatter of symbols which illustrated a considerable deviation in QS_2 from normal (represented on the graph as the zero line, or no deviation from normal). The deviations were greater in dogs exhibiting signs of heart failure with 10 dogs showing reduced, and 9 dogs an increased QS_2 .

PEP demonstrated a significant difference between the values for normal dogs and for referred cases. (Table 4.4) Fig 4.8 (b) shows this difference is mainly accounted for by the deviation from normal in dogs with heart failure. These dogs showed a marked increase in PEP while dogs with no signs of heart failure demonstrated limited deviation (mean deviation 7.66 compared with 18.66 for dogs in failure)

The LVET, despite not being significantly different between normal dogs and referred cases, is shown in Fig 4.8 (c) to be reduced in dogs with heart failure. Those dogs not in failure show less deviation from normal.

Fig 4.8 (a) - (d)

Figure 4.8 (a) - (d) : Deviations from Normal
in QS_2 , PEP, LVET and PEP/LVET in 38 referred cases.

- a) QS_2
- b) PEP
- c) LVET
- d) PEP/LVET

In all graphs, each symbol represents the mean deviation from normal in one dog. A distinction has been made between dogs which were considered on clinical examination, to be compensating and those which were in heart failure.

The y - axis represents the deviation in milliseconds from the expected systolic time interval (see Section 4)

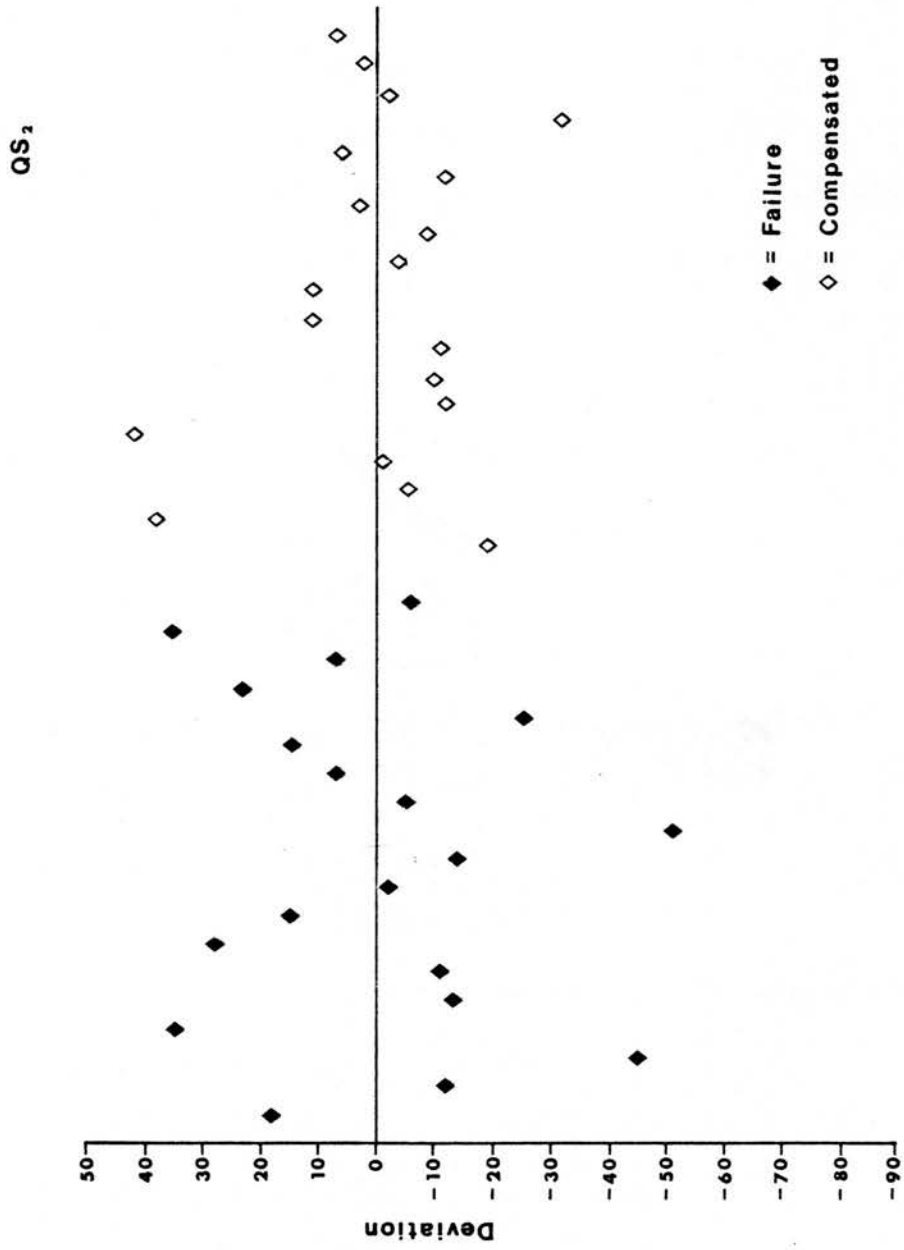


Figure 4.8 (a)

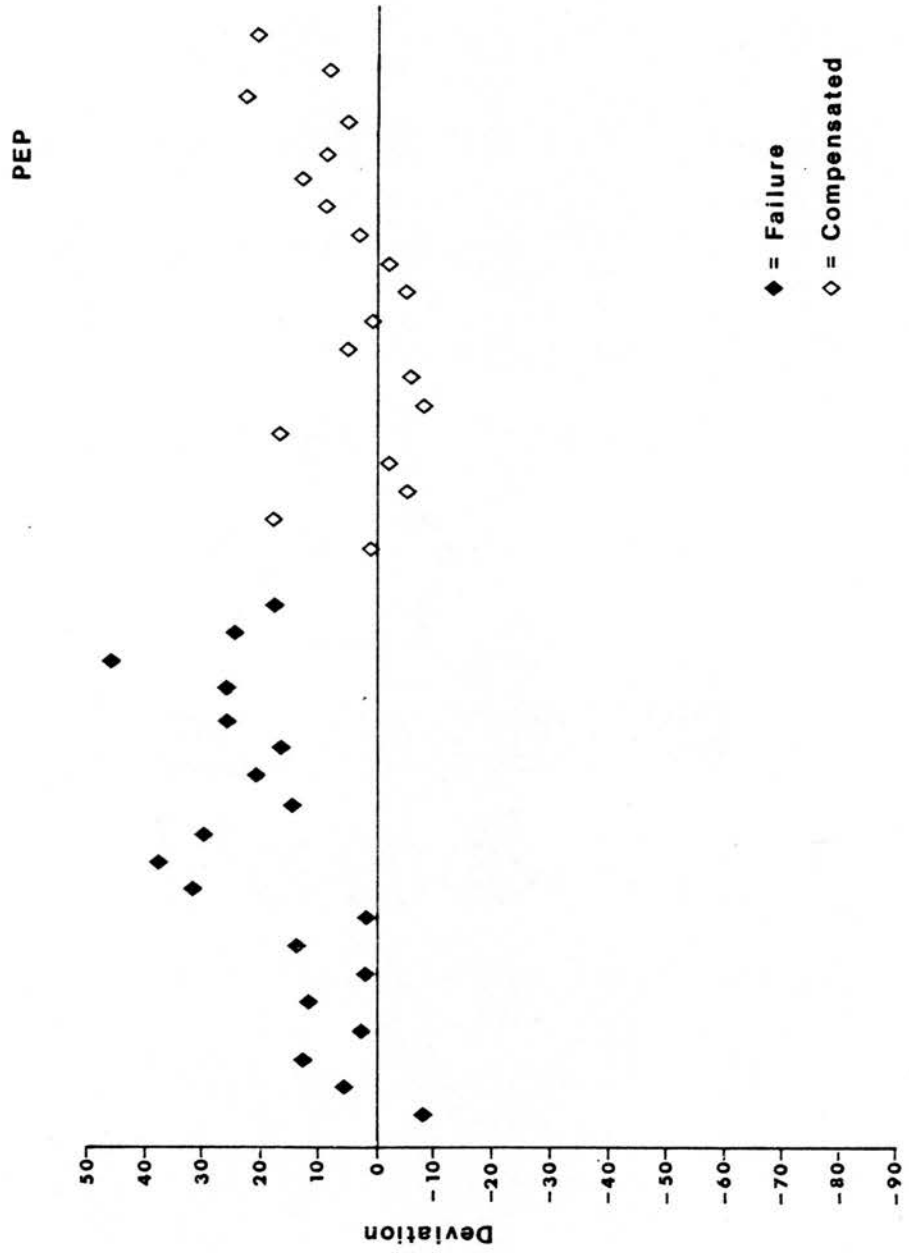


Figure.4.8 (b)

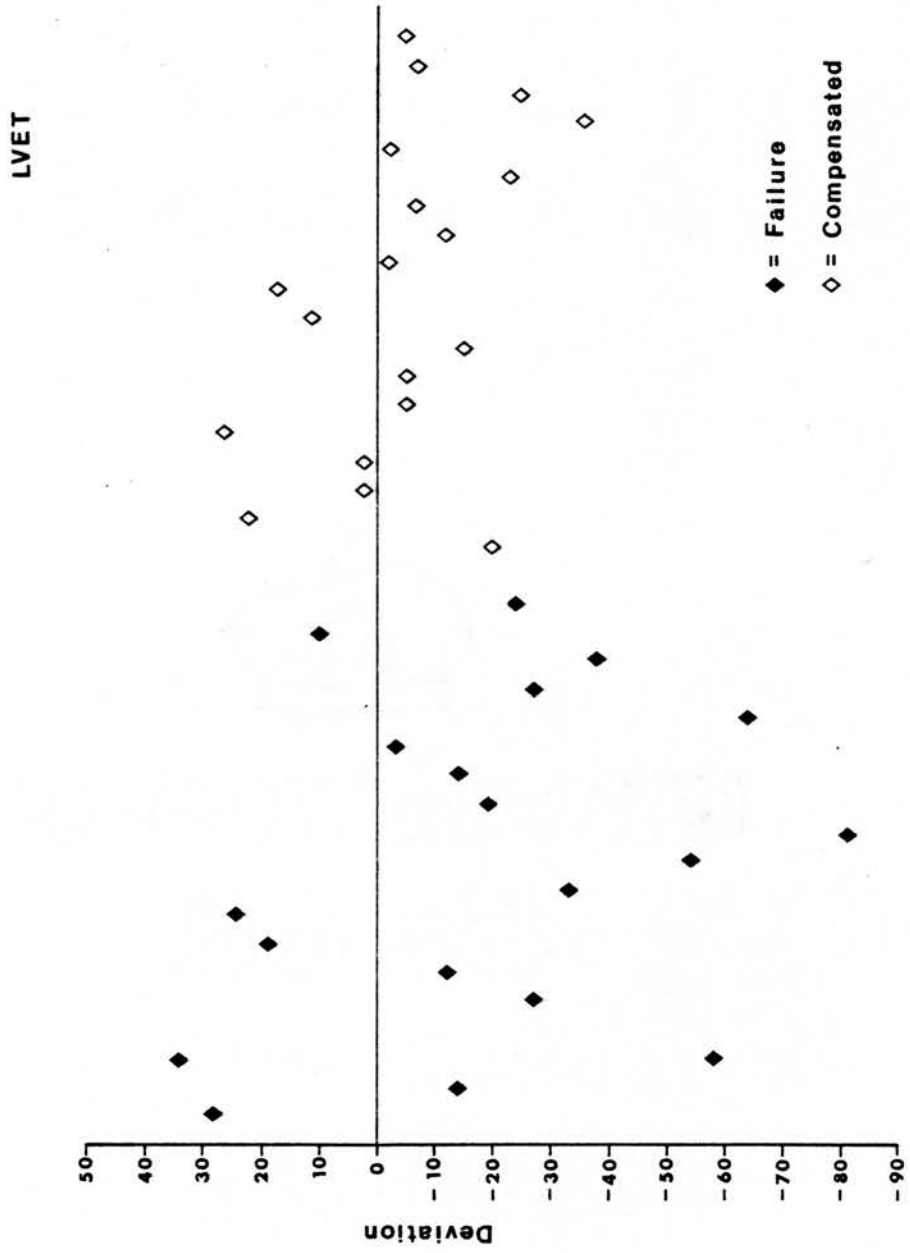


Figure 4.8 (c)

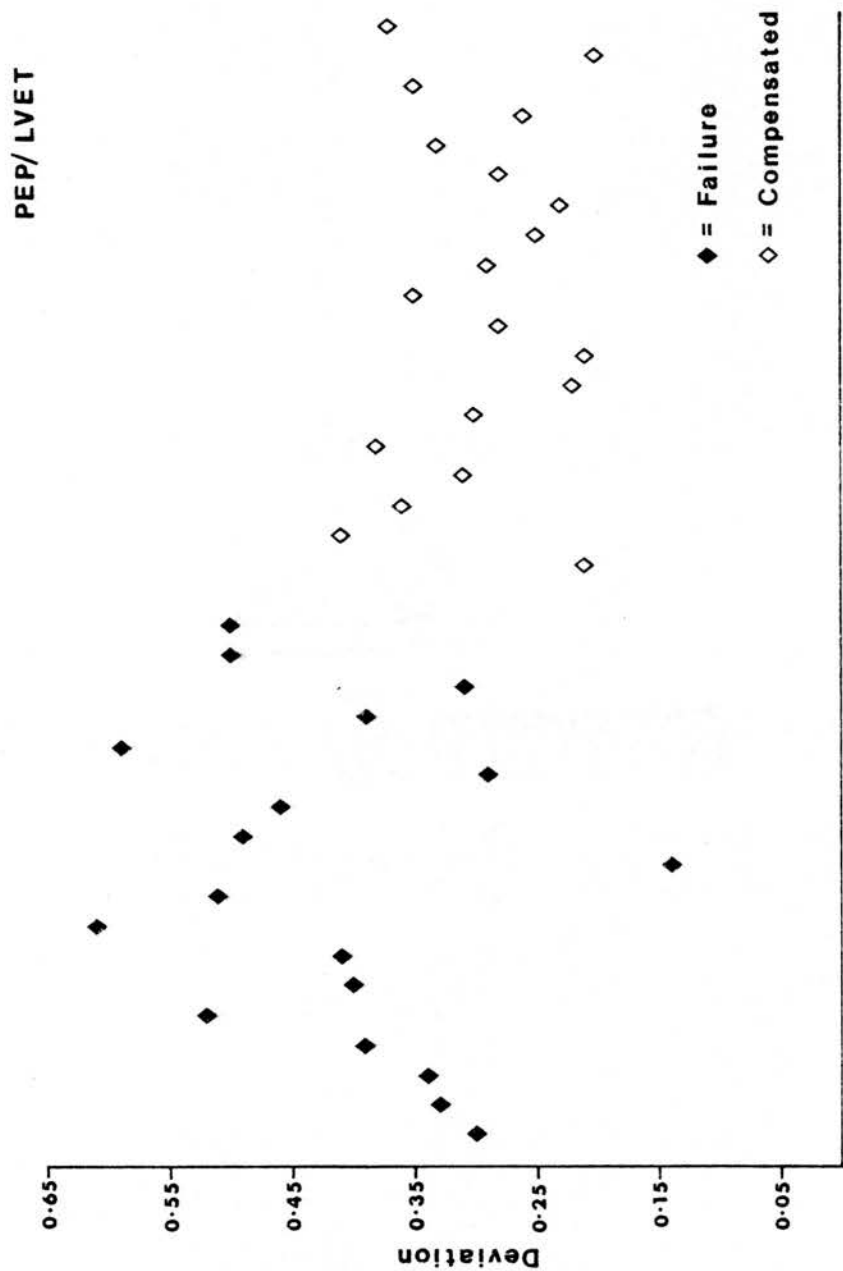


Figure 4.8 (d)

4.4 Discussion

4.4.1 Recording Procedure

Since it was not possible to use the Siemens-Elema equipment (Section 3.2.2) outwith the laboratory, another ACG machine was required for clinical recording. This was selected with the criteria stated in Section 3.4.1.

The transducer used with this equipment employed a piezo-electric crystal as already described, but the pick-up head was an air-filled capsule which avoided the problems of air leaks (Section 3.4.1). The time constant of this system was three seconds, which is considered to be satisfactory for adequate recording of ACGs (Craigie, 1975).

The recording procedure was identical to that described in Section 3.2.3. Long appointment times (90 minutes) were employed to allow the dog to accustom itself to its surroundings and to minimize adrenergic activity. Initial tachycardia usually slowed to acceptable levels for ACG recording.

Some ACGs were excluded from this study because of lack of clarity in the ECG, PCG or ACG. However, many of these recordings would be suitable for clinical use where delineation of the landmarks might need to be less clear.

4.4.2 Recording of the ACG in Various Breeds

It was possible to record ACGs of suitable quality for this study in thirty-eight dogs out of a total of sixty-one conscious dogs. However, problems were posed by the following factors.

a) Temperament - gentle manual restraint was usually adequate to

allow several recordings of the ACG to be made, but certain breeds were more restless than others. Labradors, despite their usually calm demeanour, seemed to resent having to lie quietly while recording took place. It required great patience to persuade exuberant Boxers to lie in the required position. Highly-strung Spaniels tended to show violent muscle tremors. Cavalier King Charles Spaniels were better in this respect than Springers or Cockers.

b) Conformation - the smaller breeds such as Poodles, Collies and small Cross-breeds were easily handled and provided the dog was not obese, or prone to muscle tremors, then ACGs could be successfully recorded. Large size was not a problem if the animal was well trained.

It was important in narrow-chested dogs, such as Whippets, Greyhounds, Setters and Afghans, to ensure correct placement of the transducer in the intercostal spaces. The prominent ribs in these dogs, if thin, could give rise to many artifacts, especially if the transducer moved across the ridges during respiration.

The barrel-chest of a Bull Terrier, well covered with muscle, posed little problem if the dog lay still. However, the waveform was easily lost on movement of the dog, reflecting the barely palpable apex beat.

c) Hair coat - a heavy hair coat sometimes interfered with placement of the transducer, flush with the thorax. In one dog, a Shetland Collie, it was necessary to clip the hair over the point of maximum apical beat.

The short coats of Labradors, Boxers and Bull Terriers would sometimes produce extraneous noise on the PCG. This could be reduced by dampening the hair over the area of recording.

4.4.3 Discussion of Results

The regression equations derived from data in normal, conscious dogs (Group B, Section 3) provided a basis for comparison with the STI from referred cases. In man, STI established by Weissler, Harris and Schoenfeld (1968) have been widely used as the normal values with which the STI from cardiac patients have been compared (see Section 5.1).

Alterations in QS_2

The present study showed a significant difference between the values for QS_2 obtained in normal, conscious dogs (Group B) and those from referred cases (Table 4.4). This result was at variance with the finding that QS_2 is altered minimally by heart disease in humans (Weissler, Harris and Schoenfeld, 1969; Lewis et al, 1974; Lewis et al, 1977)

QS_2 showed both shortening and prolongation, with the dogs in clinical heart failure showing much greater deviations from the expected norm (Fig 4.8 a). QS_2 intervals from three dogs in failure (dogs nos. 60, 72, 79) were increased ($> +1SD$) and reflected not only a longer PEP but also an increased LVET. Despite the large ventricular stroke volume which occurs in mitral regurgitation, prolongation of the LVET rarely occurs in man (Garrard, Weissler and Dodge, 1970) and the ejection time is characteristically foreshortened. An explanation of this increase in LVET (vide infra) relies on assumptions made about haemodynamic measurements (eg. blood pressure and end-diastolic volume) which are not readily available in non-invasive studies.

Three dogs in failure (dogs nos. 42, 43, 76) had QS_2 intervals which were shorter than the expected norm. These dogs each had an increased PEP, but the main alteration was a marked shortening of

the LVET (deviations from normal were -64, -81 and -58 respectively). Two of these dogs had mitral regurgitation and one was in atrial fibrillation. The PEP/LVET for these dogs were increased (0.59, 0.49 and 0.34 respectively) suggesting, as does the reduced LVET, a diminished cardiac output.

Two dogs (nos. 52 and 70) which were not considered to have clinical heart failure demonstrated an increase in QS_2 , PEP, LVET and PEP/LVET. These STI indicate some degree of myocardial malfunction despite there being no overt signs of heart failure. An ECG taken from dog no. 52 showed atrial premature beats.

The QS_2 is regarded as being a constant, despite cardiac malfunction (Lewis et al, 1977). Early work by Wiggers (1921) in the dog suggested that an augmented stroke volume effectively reduced the duration of total systole. However, this was not confirmed by Wallace et al (1963) who found that total systole was reduced by

- a) increased heart rate
- b) increased sympathetic activity
- c) digitalis

They concluded that altering stroke volume and aortic blood pressure had no consistent effect on the duration of total systole which remained unchanged or little altered.

The QS_2 (total electromechanical systole) is considered to be decreased by positive inotropic agents and increased by the following factors:

- a) left ventricular conduction defect

b) aortic valve disease

c) acute increases in arterial blood pressure (Lewis et al, 1974)

It is possible that during the time of recording or as a result of the mitral regurgitation, the aortic blood pressure was raised in those showing an increased QS_2 . An increase in afterload is responsible for increasing the PEP and LVET also and could contribute to the observed increases in these intervals. An explanation for reduced QS_2 values has not been found beyond the recording of a concurrent decrease in LVET and possible adrenergic stimulation.

If the QS_2 values for referred cases (disregarding the highly deviant values just discussed) are compared to normal QS_2 values then the QS_2 was altered very little between dogs with and without heart failure. This reflects the situation in man where the QS_2 remains unaltered despite changes in PEP and LVET.

Alterations in LVET

The LVET values between normal and referred cases did not differ significantly. However it is clearly demonstrated in Fig 4.8 (b) that the ejection times for the majority of dogs in failure were markedly reduced. This is one of the characteristic changes in STI which occur in left ventricular decompensation, when the left ventricle is functioning under a volume overload.

This decrease in LVET is more complex to explain than the accompanying increase in PEP. One factor may be that the increase in PEP (due to a diminished rate of left ventricular pressure rise) delayed the onset of ejection. LVET may be reduced by increasing aortic blood pressure in the dog (Wallace et al, 1963). Myocardial contractility is augmented by an increase in blood pressure (Rushmer, 1976) and by increased heart rates, but the fundamental

lesion in myocardial failure in a reduction in the intrinsic contractility of the myocardium (Henderson, 1975). As the failing ventricle becomes distended, the velocity of fibre shortening is reduced which might be expected to produce a lengthening of the LVET. However, the extent of fibre shortening is also reduced in the LVET (Lewis et al, 1977).

Henderson (1975) suggests that the ejection phases may be more use for diagnosis, since it avoids the problems inherent in isovolumetric analysis.

Alterations in PEP

Fig. 2.8 (c) shows that the significant increase in PEP in referred cases in this study was mainly accounted for by a deviation in dogs showing clinical signs of heart failure.

One dog (no. 79) in failure had a shorter PEP than expected. A reduced PEP is seen in acute myocardial ischaemia in man and experimental dogs (Section 3.4.4) and also during increased sympathetic activity. However, the most likely reason for this decrease in PEP is the positive inotropic effect of digoxin on the myocardium (this dog had been receiving digoxin for two months at the time of recording). Two dogs (nos. 45 and 61) not in heart failure were also receiving digoxin and demonstrated PEPs shorter than expected by deviations of -2 and -8 respectively.

A prolongation of PEP is generally attributed to a diminished rate of left ventricular pressure rise during isovolumic systole. The isovolumic contraction time is measured as SUT on the ACG. While Q-C (electromechanical delay) was only marginally increased in clinical cases, the SUT demonstrated a marked increase at heart rates up to 170 beats/minute (Fig. 4.1 d). A close correlation between SUT and

the internal indices of left ventricular function (IVCT, dP/dt , $t-dP/dt$, V_{pm}) have been found in man (Manolas, Wirz and Rutishauser, 1976) and in experimental dogs (Tally, Meyer and McNay, 1971). The results in this study suggest that within the heart rate range 70-170 beats/minute, the prolongation of PEP results from an increase in SUT, which may reflect reduced myocardial performance.

Alterations in PEP/LVET

The PEP/LVET demonstrated a significant increase in the ratio calculated in referred cases. The PEP/LVET has been found in man to remain within narrow limits among normal subjects, even when uncorrected for heart rate (Weissler, Harris and Schoenfeld, 1969). The ratio has been shown to correlate well with the ejection fraction in man (Waagstein, Hjalmarson and Wasir, 1974) in a number of cardiac diseases including cardiomyopathy and mitral valve disease. It has been suggested that PEP/LVET is a more sensitive index of left ventricular dysfunction than either the cardiac index or stroke index (Lewis et al, 1970). Ahmed et al (1972) concluded that this ratio, like PEP, can indicate the contractile state clinical heart failure, provided the lesion is confined to the myocardium.

In this study, the PEP/LVET in referred cases did not demonstrate a significant relationship with heart rate. Figure 4.8 (d) demonstrates the increases in PEP/LVET ratio observed in dogs with heart failure. Those dogs not in failure also demonstrated a ratio which was higher than expected. This perhaps is a reflection that these dogs, although considered to have no cardiovascular abnormality, may indeed have had some measure of left ventricular dysfunction to account for the presenting signs.

4.4.4 Apexcardiography in Clinical Situations

Eight dogs out of thirty eight referred cases (in which ACGs were recorded) were considered to have no obvious cardiovascular abnormality on clinical examination. STI from these eight dogs were compared with the normal data from Group B. No significant difference was found between the two groups, suggesting that the eight referred cases had STI representative of Group B (normal) dogs. However, statistically this small group could not be considered as a random sample of the normal population since the selection was made from dogs presented at the clinic and more specifically from dogs with possible heart disease.

When the individual STI were examined for these eight dogs, three dogs (nos. 56, 63, 73) were found to have a prolonged PEP. Dog no. 63 had previously had total atrioventricular block with left bundle branch block but was in sinus rhythm at the time of STI measurement. Of the other two dogs, no. 56, a Greyhound had a history of exercise intolerance and no. 73, a Labrador presented with several episodes of syncope. Both dogs also had a notably reduced LVET. The PEP/LVET for these dogs were increased. Although an increase in this ratio does not of itself constitute definite evidence for a failing ventricle (Weissler, Harris and Schoenfold, 1969) the deviations from normal in the other STI suggests that the presenting signs are perhaps of cardiovascular origin. No serial STI were available and therefore it was not possible to determine the consistency of these results.

Atrial Fibrillation

ACGs were recorded in five dogs with atrial fibrillation (AF). However, the apex waveforms were extremely irregular reflecting the chaotic apical beat felt at the precordium. In only one dog (no. 42) were the landmarks for STI measurement clearly defined over five consecutive beats. Measurement of STI presented certain problems.

For example, the RR intervals vary widely from beat to beat thus not meeting the criterion that RR intervals should vary by less than 10 msec. (see Section 3.2.4) It has been suggested that the duration of LVET (Schoenfeld et al, 1963) and the PEP (Lewis et al, 1974) in man are related to the preceding RR interval in AF. PEP and LVET were calculated in relation to the preceding RR interval in this study.

PEP was found to lengthen rather than decrease with shortening RR intervals which was in agreement with the results of Sherman and Lewis (1972). It has been suggested that beats following a short RR interval function under a diminished preload and a greater isovolumic pressure must therefore be generated. This would account for the relative prolongation of the PEP (Lewis et al, 1974).

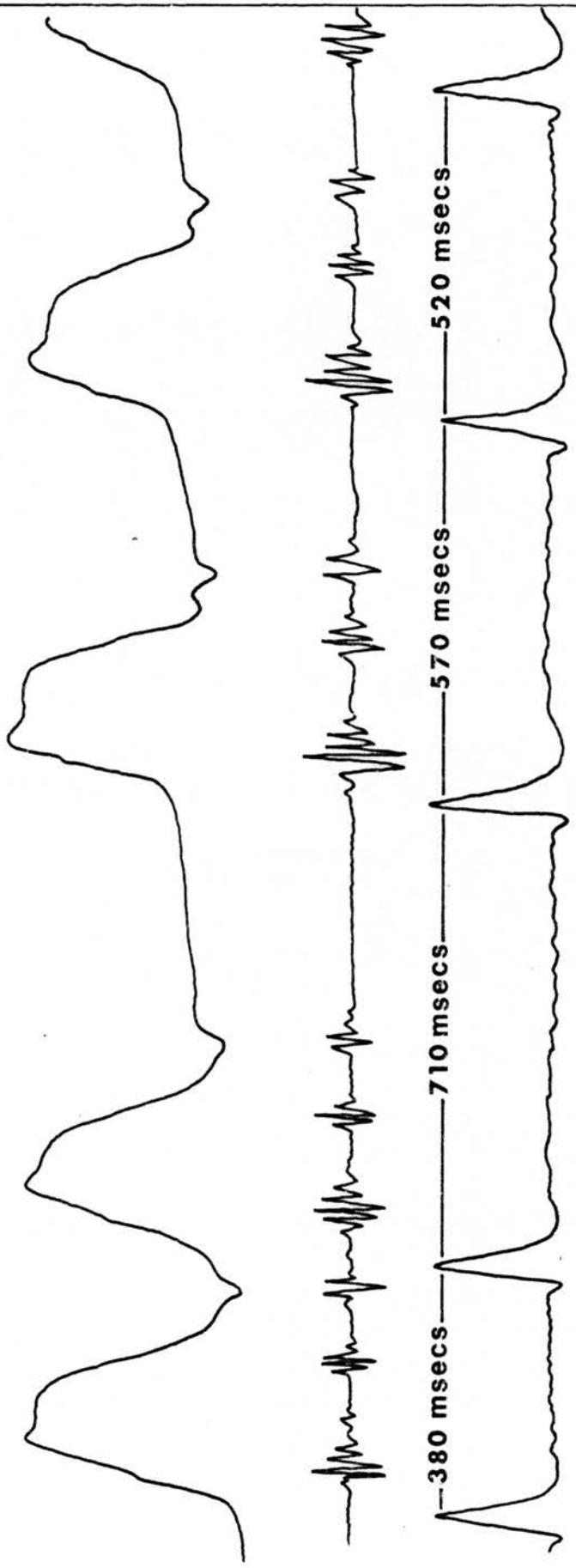
LVET and PEP/LVET in this dog were increased. The inclusion of too many beats with short preceding RR intervals in STI estimation can lead to a falsely high PEP/LVET (due to the lengthening of PEP in these beats). Lewis et al (1974) suggest measurement of STI only in beats with RR intervals below 800 msec to avoid underestimating potential myocardial performance. In this study consecutive beats suitable for STI measurement were so few that selection of beats of specific RR intervals was not possible (Fig. 4.9).

It must be concluded that apexcardiography is not the technique of choice for determining left ventricular function in AF. Recent advances in echocardiography allow more accurate assessment of contractile function in this condition in dogs (Wingfield, Boon and Miller, 1982; Lombard, 1984).

Other Dysrhythmias

One dog (no. 63) had total atrioventricular block with left bundle branch rhythm (Fig 4.5). Beats which escaped the atrioventricular

Figure 4.9.



Variations in RR Interval as a Result of Atrial Fibrillation.
Recording taken at 100mm sec⁻¹.

block produced an apex wave but difficulty was encountered in correcting STI for heart rate since meaningful RR intervals were not available.

Atrial and ventricular premature beats were encountered in four dogs with mitral incompetence and in two dogs as the only clinical abnormality. The dysrhythmia in these dogs was intermittent and STI could be measured from normal sinus beats. Ectopic beats resulted in an apex wave of indeterminate morphology and thus the STI could not be measured. The beat following the extrasystole (and compensatory pause) demonstrated a shorter PEP and a longer LVET than normal beats as in man (Lewis et al, 1974). This was probably as a result of the increased length of diastole, resulting in an increased diastolic ventricular volume and therefore an enhanced stroke volume (Frank-Starling mechanism). Postextrasystolic beats were not used in STI calculation.

Valvular Lesions

Measurement of STI in man appear to be most useful in evaluation of myocardial dysfunction but some information is available for comparison with this study.

Aortic Stenosis

Apexcardiograms suitable for STI measurement were found in one dog (no. 53) with a confirmed diagnosis of aortic stenosis. The dog was in clinical heart failure and an abbreviated LVET might have been anticipated (Section 1.8) but the ejection time was longer than expected. Studies in man have indicated that severe aortic stenosis is accompanied by a prolongation in LVET (Benchimol, Dimond and Shen, 1960). The PEP is usually shortened which results in an increased PEP/LVET. In this dog, the PEP was prolonged - a recognised change in patients with aortic stenosis following left ventricular decompensation (Lewis et al, 1974). Failure may produce the

expected decrease in LVET.

Prolongation of LVET in aortic stenosis may be as a result of early opening and late closure of the aortic valve. There is a delay in the inscription of the incisural notch on the carotid arterial pulse and the aortic component of the second heart sound (A_2). Luisada, Bhat and Knighten (1978) have shown A_2 to be coincident with the closure of the aortic valve in dogs. The delay in inscription of A_2 might account for the prolonged QS_2 recorded in this dog. It has been suggested that altered flow patterns during ejection and the post-stenotic dilatation of the aorta (resulting in reduced aortic pressure) may be responsible for the delay (Lewis et al, 1974).

Treatment of left ventricular failure in aortic stenosis results in shortening of the PEP (and lengthening of the LVET). The decreased PEP, seen in aortic stenosis without concomitant failure, is probably due to the rapid rate of rise of left ventricular pressure and a relatively small isovolumic pressure gradient since the aortic diastolic pressure is low (Lewis et al, 1977).

More than one case is required to assess the usual effect of aortic stenosis on the STI in the dog. However, QS_2 and LVET were difficult to obtain due to the pronounced systolic ejection murmur obscuring S_2 .

Pulmonic Stenosis

This condition causes relative obstruction of the right ventricular outflow and often presents without clinical signs. The effect on the left ACG is therefore expected to be minimal.

In this study, three dogs (nos. 51, 64, 66) with a proposed diagnosis of pulmonic stenosis were examined. One further dog (no. 75) had pulmonic stenosis and a ventricular septal defect confirmed

at post mortem examination. If the STI indices for these four dogs are examined, the deviations from the expected normal (Table 4.6) show that dogs nos. 51 and 64 had normal STI (within $\pm 1SD$).

Table 4.6 : Deviations from Normal in Dogs with Pulmonic Stenosis

Dog No.	C/F	QS ₂	Deviations		
			PEP	LVET	PEP/LVET
51	C	+ 11	- 5	+ 17	+ 0.35
64	C	+ 7	+ 1	+ 11	+ 0.28
66	F	+ 7	+ 46	- 38	+ 0.82
75	F	+ 23	+ 25	- 27	+ 0.39

The two dogs in heart failure demonstrated expected lengthening of PEP and decrease in LVET.

These results suggest that the STI are not affected in pulmonic stenosis unless left ventricular decompensation ensues when the expected changes in STI occur.

Mitral Incompetence

The majority of dogs examined in this study had evidence of mitral incompetence as the major cardiac lesion. Nine dogs with mitral incompetence and in cardiac failure had a prolonged PEP and reduced LVET (Table 4.2). In man, these changes in STI occur as a result of a) the haemodynamic effect of mitral regurgitation and/or b) the diminished contractile performance of the left ventricle. These alterations are emphasized in left ventricular decompensation. A prolonged PEP may be associated with inadequate preload coupled with reduced diastolic compliance, a possible consequence of chronic left ventricular overload (Lewis et al, 1977).

In this study, four dogs in failure did not show the alterations in PEP and LVET mentioned above. All four had a longer LVET than normal, two with normal PEP, one having a reduced PEP and one with an increased PEP despite a large left ventricular stroke volume, a prolonged LVET is uncommon in man (Garrard, Weissler and Dodge, 1970).

The role of left ventricular function is important when interpreting the STI values. From the small group of clinical cases studied, it is difficult to draw any conclusions. Data on the ventricular volumes and pressure during recording are not available and therefore explanations for left ventricular dysfunction in mitral incompetence relies on other studies (Pensinger 1968; Myer and Bonagura, 1982; Kittleson et al, 1984).

The initial problem of mitral incompetence is regurgitation of blood into the left atrium during systole. In chronic mitral incompetence, hypertension develops in the left atrium, pulmonary capillary bed and pulmonary arteries. The left ventricle functions under a volume overload which causes both dilatation and hypertrophy (vide supra). The end-diastolic volume increases markedly with little or no increase in end-diastolic pressure until heart failure ensues.

The finding of abnormal STI (prolonged PEP, reduced LVET and increased PEP/LVET) is strongly suggestive of abnormal left ventricular function in mitral regurgitation (Lewis et al, 1974). Lewis et al (1977) suggested that in man a normal PEP/LVET in mitral incompetence provides evidence for a well compensated ventricle whereas an increase in PEP/LVET of 0.5 or greater may signify left ventricular decompensation.

In this study the mean deviation from normal for dogs in failure was 0.46 while the mean deviation for those dogs not in failure was 0.31 which suggests that PEP/LVET may be a valuable indication of decompensation in dogs.

The use of diuretics to relieve congestive heart failure may disguise the severity of the underlying left ventricular dysfunction. In this study, dogs in failure demonstrated abnormal STI while STI from those considered to be compensating well, and with probable normal left ventricular function were not markedly altered. This suggests that the STI do not indicate cardiac dysfunction which is not clinically obvious and that they are therefore of value in supporting a proposed diagnosis of cardiac failure.

4.4.5 The Effect of Drugs on STI

Inotropic Drugs

The abbreviation of the STI during inotropic drug administration has been well studied (Lewis et al, 1972) and QS_2 has been shown to be most sensitive to inotropic stimulation. In this study, of three dogs (nos. 45, 61 79) receiving digoxin at the time of recording, one had an increased QS_2 , one was unaltered and one showed a marked decrease in this interval. It was noted that, of these three dogs, only one was in clinical heart failure and this was accompanied by a prolonged QS_2 . This result might suggest that the dog was under-digitalised.

The PEP in dogs is decreased by positive inotropes (Tally, Meyer and McNay, 1971) and it has been suggested that this alteration may be useful to monitor the level of inotropy. This was not found to be the case in one dog study (Gross et al, 1974). In this study, all the dogs receiving digoxin demonstrated small reductions in PEP (-8, -2, -8).

The response in LVET was more variable, only one dog (no. 45) showing the expected abbreviation of this interval. LVET in dog no. 79, which was in clinically overt failure, was markedly lengthened. These inconsistencies are in agreement with Gross et al's study (1974) in normal conscious dogs. In man, the response in LVET to cardiac glycosides was found to be variable in patients with heart failure.

The PEP/LVET in this study showed a small, but consistent increase (0.30, 0.34, 0.30) in dogs receiving digoxin. The PEP/LVET is affected less than PEP or LVET alone. The effects of heart failure on the STI are rarely completely reversed and so it is common to observe an increased PEP/LVET in patients on a maintenance dose of glycoside (Lewis et al, 1974). This possibly suggests that PEP/LVET is an indication of left ventricular function despite the therapeutic effects of digoxin.

Beta - blockers

Two dogs with atrial fibrillation were receiving the beta - blocker, propranolol but quality ACGs could not be recorded for the reasons stated in Section 4.4.4. In man, propranolol causes lengthening of PEP while other beta blockers have no effect, or cause a slight shortening of this interval (Lewis et al, 1974). However, Waagstein et al (1974) found that practolol increased the PEP to normal values during acute myocardial infarction. The explanation for these changes has not been elucidated. It has been suggested that propranolol has a depressent effect on the myocardium, despite causing a decrease in LVET (Lewis et al, 1974).

Alpha - blockers

The alpha - blocker, prazosin, was the treatment of choice for four dogs in this study. However, follow-up ACGs were not available for STI measurement. In man, the effect of phentolamine, another alpha-blocker, is to cause a significant shortening of PEP and LVET lengthening. The former effect might suggest a positive inotropic effect on the myocardium.

SECTION FIVE

GENERAL DISCUSSION

PROJECTED STUDIES

AND

CONCLUSIONS

5.1 General Discussion

This study was designed to allow the measurement of STI from a reasonably large number of dogs. Beagles presented for experimental cardiac surgery over a two year period formed the population in Section Three.

Good quality ACGs were recorded from most of these dogs for inclusion in the study, thus avoiding the pitfalls of random selection. The STI measured from Group A (normal dogs) were used for comparison with STI from some of these dogs following coronary artery ligation (Group C). The STI collected from Group B (conscious dogs) were used for comparison with STI from referred cases in Section Four. Some of these dogs were in clinical heart failure.

The interpretation of results is critically dependent on the circumstances under which recordings are made (Gibson, 1975) and inaccuracies may result from extrapolation of data outwith the original population. In man, STI regression equations established by Weissler et al (1968) have been widely accepted as standards by other experimental and clinical laboratories. Assuming that the equipment is adequate for STI measurement, then this comparison is viable, given the small variation in chest conformation in man.

Direct comparison of canine STI with STI from man is not possible. The Y - intercepts and slopes of the regression equations demonstrate marked differences in value. However, parallels can be drawn and general trends contrasted:

a) Both species show a strong inverse relationship of heart rate to QS_2 and LVET. PEP demonstrates a weaker relationship in man and in dogs in this study. However, Pipers et al (1978) reported that PEP was independent of heart rate in their study, involving a small number of dogs;

- b) PEP/LVET in dogs shows a positive correlation with heart rate (Pipers et al 1978; this study) while in man it is independent of heart rate (Lewis et al, 1974);
- c) The presence of heart failure appears to cause prolongation of PEP and a decrease in LVET in both species;
- d) In both species, the PEP/LVET may identify left ventricular dysfunction when either PEP or LVET (or both) are within normal limits.

In this study, STI from normal conscious Beagles were used for comparison with referred cases. Certain points emerged which might cause the validity of such a comparison to be questioned. These are as follows:

- a) The population samples were different ie. normal Beagles were compared with dogs of many different breeds;
- b) Referred cases encompassed many dogs showing great variation in thoracic conformation;
- c) Dogs of diverse temperaments responded differently to stressful situations.
- d) Referred cases were unfamiliar with the recording procedure and were therefore less easy to handle.
- e) The recording equipment was different, albeit selected carefully in both situations to be as comparable as possible (Section 3.4.1)
- f) The recording procedure took place at differing times during the

day (Sections 3.2.2 and 4.2.1). The effect of diurnal variation on the STI has not been studied in the dog but it may have an effect on autonomic control of the heart.

The importance of establishing baseline data for a particular technique is emphasized. Pipers et al (1978) used echocardiography and the carotid arterial pulse to obtain STI. The regression equations obtained by these techniques differed from the STI in this study. This is evidence to suggest that for each technique (eg. ACG, carotid pulse, echocardiography), routine (ie. experimental or clinical), and set of equipment used, a range of normal STI should be instituted. Calculation of STI indices indicates the deviation from the expected norm (for that particular situation) and these values can be used for inter-laboratory comparison.

Results which correlated well with STI abnormalities observed in cardiac failure in man (Section 4.4) were obtained in this study. However, in the interpretation of STI in clinical situations, the advantages of serial measurements have been stressed (Lewis et al, 1977). Results in this study would have been more meaningful if sequential ACGs had been recorded on a before and after treatment basis. Certain dogs had ACGs recorded from them on more than one occasion. Two problems were encountered in serial comparisons:

- a) Quite often quality ACGs were not obtained from dogs in severe heart failure due to pronounced dyspnoea (Section 4.3.1). Following treatment, good ACGs could be recorded.
- b) Short out-patient, re-appointment times often precluded satisfactory ACG recording due to tachycardia (Section 4.4.1). Foreknowledge of the recording procedure may have contributed to this adrenergic stimulation.

From a practical viewpoint, recording of serial ACGs would require hospitalisation of the patient for satisfactory ACG recording.

5.2 Projected Studies

Further work might include:

a) Serial STI in dogs:

- (i) in normal dogs to assess the effect of diurnal variation, if any, on STI.
- (ii) as an assessment of myocardial dysfunction underlying congestive heart failure or in clinically unaffected dogs with heart disease.
- (iii) to monitor the therapeutic effect of treatment eg. diuresis alleviating the signs of congestive heart failure, or the inotropic effect of digoxin.

b) Inter-breed comparison of STI.

Recording of STI from normal dogs of varied breeds and conformation would establish further baseline data against which dogs with various types of cardiac disease might be compared. An interesting extension would be to examine sufficient normal dogs of each breed to define the STI parameters for the breed. The validity (or otherwise) of inter-breed comparisons (for example, STI from a greyhound compared with STI from a poodle) might then be verified.

c) Use of other techniques with, or instead of, the ACG.

The problems encountered in STI measurement from the ACG are stated in Section 4.3.1. The use of echocardiography obviates many of these problems and while it is another non-invasive technique, it still requires very expensive equipment.

The technique has been used in dogs in order to visualize the anatomical structures of the heart in motion (Thomas, 1984). The echocardiographic trace at the level of the aortic root demonstrates the cusps of the aortic valve and their excursions during the cardiac cycle (Pipers, Andrysko and Hamlin, 1978). M-mode echocardiography allows a visual display of cardiac motion as a function of time and superimposition of an ECG permits measurement of STI, obviating the need for ACGs and PCGs. One obvious advantage in clinical situations is in dysrhythmias such as atrial fibrillation (Section 4.4.4) and in certain dogs where, for example, the PCG is obliterated by a pan-systolic murmur. Echocardiography has been used successfully to assess left ventricular function in dogs with atrial fibrillation (Wingfield, Boon and Miller, 1982; Lombard, 1984).

The technique has been used in man in conjunction with the carotid arterial pulse (Vredevoe, Creekmore and Schiller, 1974) and the ACG (Venco, Gibson and Brown, 1977) for timing left ventricular events.

Simultaneous recordings of the ACG, ECG and PCG with echocardiography would allow accurate non-invasive measurement of STI in the presence of dysrhythmias and pan-systolic murmurs. The ACG would permit further measurement of the PEP. Echocardiography has been used to demonstrate ventricular dilation and hypokinesis (Lombard, 1984).

No single non-invasive test yields useful information with regard to cardiac function but simultaneous records of several techniques offer a quantitative estimate of cardiac performance when used in conjunction with traditional clinical diagnostic aids.

d) Use of the ACG in other Species.

During the course of this study, ACGs were incidentally recorded in ten cats. Two problems were encountered:

- (i) If the cat started to purr, the first and second sounds were obscured on the PCG. This actually occurred infrequently, the attachment of ECG leads being sufficient to inhibit purring in most cats.
- (ii) One of the presenting signs of heart failure in the cat is dyspnoea and if severe, this could interfere with ACG recording.

Mostly the traces of ECG, ACG and PCG were of excellent quality and clearly defined the points for STI measurement. Cats appeared to be more favourable subjects for ACG recording than dogs. They have a reasonably consistent thoracic conformation, relatively low incidence of obesity and absence of panting, all of which assist in recording clear ACGs.

Considering the high incidence of myocardial involvement in cardiac disease and the relative lack of pathognomic signs of cardiac failure in cats, STI might prove to be a useful technique for assessment of left ventricular dysfunction in this species.

5.3 Conclusion

Apexcardiography provides a readily - applied, non-invasive record of the mechanical function of the heart. However, certain inaccuracies are inherent in the recording and measurement of the trace (Section 3.4).

STI measurement requires simultaneous clear records of the ECG, PCG and ACG from at least five consecutive beats. This is not easily achieved in conscious, unsedated dogs. Furthermore, in certain dogs (eg those which are obese, have massive left ventricular hypertrophy, a dominant dysrhythmia or severe dyspnoea) it was impossible to record a legible ACG.

The STI measured from normal, anaesthetised dogs fall within narrow limits relative to heart rate. QS_2 , PEP and LVET show an inverse relationship to heart rate over the range 90-190 beats/minute. A significant positive correlation of PEP/LVET with heart rate was noted.

Individual and group variation increased in STI from conscious dogs. However, a similar clear relationship of QS_2 , LVET, PEP and PEP/LVET to heart rate was recorded.

Pentobarbitone anaesthesia had a significant effect on the STI in dogs in this study, resulting in prolongation of QS_2 , PEP and LVET, and a slight increase in PEP/LVET. This suggests that STI from anaesthetised dogs should not be used as the basis for comparison for STI from conscious dogs, and vice versa.

STI from dogs with experimentally induced myocardial infarction demonstrated no significant differences from STI recorded in normal dogs. These dogs showed no signs of clinical heart failure, despite large areas of myocardial ischaemia evident post mortem. It must be concluded that the STI failed to indicate the underlying left

ventricular dysfunction in the absence of clinical signs.

Recording of the ACG in dogs of various breeds proved that STI measurement was possible in the majority of cases. The STI were found to deviate from normal in the presence of heart failure, regardless of cause. In general, the PEP lengthened and the LVET decreased as a result of decompensation. The QS_2 did not always remain constant; possible explanations for this have been discussed. The patterns in STI deviation as a result of cardiac disease in these dogs correlated well with the classical deviations described in human patients.

Deviations in PEP and LVET may be useful in furthering a diagnosis of decompensation. PEP/LVET appeared to be a more sensitive indicator of underlying cardiac disease and could aid prognosis in the absence of heart failure.

For satisfactory measurement of STI from the ACG the following conclusions have been drawn:

- a) The technique requires the use of equipment (transducer, preamplifier and recorder) with characteristics suitable for ACG and PCG recording. This includes a known time constant (not less than 3 seconds), frequency response and phase shift (Section 3.4.1).
- b) For each technique, within each laboratory, normal STI should be established for both anaesthetised and conscious dogs. These provide a comparison for STI from dogs with heart disease;
- c) A standardised recording technique should be used. (Sections 3.2.2 and 4.2.1).
- d) Satisfactory ACG recording in conscious dogs requires considerable time and patience.

In conclusion, these studies suggest that the STI may provide valuable information about the mechanical performance of the heart when employed as part of a full clinical investigation.

APPENDICES

APPENDIX 1: Technical Data for Siemens - Elema
Mingograf 82 and Selected Preamplifiers

A Mingograf 82

Power supply: 110V/120V/220V/
240V, $\pm 10\%$, 50-60 Hz.

Paper speed: 2.5-5-10, 25-50-100,
250-500-1000 mm/s.

Recording span:

28 mm (± 14 mm) at 17 mm jet length
56 mm (± 28 mm) at 35 mm jet length
84 mm (± 42 mm) at 52 mm jet length

Frequency range: 0-1250 Hz (-3 dB)
at 17 mm jet length

Linearity: better than 3%

CMRR, final amplifier:

80 dB at 50 Hz, 10 Vp-p

X-input (final amplifier input):
nom. ± 1.4 V, 1 MOhm

Output to oscilloscope and tape recorder
nom. ± 1.4 , 10hm

C Pulse Amplifier 859

Input impedance: 80 K (adapted
for Pulse/phono Transducer 860)

CMRR: 30 dB (50 Hz)

Amplification: 1/4 - 1300 times
(adjustable with 12-step selector
and vernier control)

Time constant: 0.3, 1.6, 4, 7s

Upper frequency limit: 300 Hz
(-3 dB) at max amplification,
2500 Hz (-3 dB) at min amplification

Output impedance: 1 , unsymmet-
rical

Output voltage: 1.4 V at 110 mV_{in}
(gain selector in position 1 and
vernier control in mid position)

Output current: max 1 mA (short-
circuit protected)

Power supply: ± 19 V, consumption
 ± 15 mA, +8 V, consumption 30 mA

B EKC - Amplifier 850

Input impedance: 1000 M parallel
with 330 pF

DC-current in patient leads max 10^{-10} A
Skin potentials: max 400 mV

CMRR: 80 dB (50Hz); with input short-
circuited, without HF-filter and over-
load protection

60 dB (50 Hz); input unbalanced with
5 k , with HF-filter and overload
protection

Noise: 15 Vp-p; input loaded with
2 x 25 k , without filter

Calibration: 1 mV

Sensitivity: 2, 1, 1/2, 1/4 cm/mV
(gain 500 in position 1)

Time constant: 1.8s (option 3.2 or
0.25s)

Upper frequency limit: 120 Hz (-3 dB)
option 2500 Hz (-3 dB); decreased with
FILTER-button 30 Hz, 300 Hz (-20 dB)

Output impedance: 1

Output voltage: ± 1.4 V for ± 3 mV_{in}
(sensitivity selector in position 1)

Output current: max 1 mA

Power supply: ± 19 V, consumption 15 mA

D Normalizer 869

Input impedance 200 kohms

Output impedance: 1 ohm $\frac{dA/dt}{A}$ and dA/dt

2 kohm for apex pulse A

Calibration: ± 0.25 V (corresponds to $\pm 10s^{-1}$)

Supply voltages: ± 19 V

Current drain: 80 mA

Dimensions: Width 54.5 mm (1/8 module)
Height 177 mm
Depth 200 mm

Weight: 0.8 kg

E Phono amplifier 858

Input Adapted for microphones 25C (61 04 012 E049E)
and 26 (61 04 020 E050E)

Noise (referred to input,
filter Ph6) 30 V (p-p)

Sensitivity 1-1/2-1/5-1/10-1/20-1/50-1/100 and 1/200

Frequency response

Filter	Max amplitude	Roll off	
		positive flank	negative flank
Ph1	25 Hz	18 dB/octave	-6 dB/octave
Ph2	50 Hz	18 dB/octave	-6 dB/octave
Ph3	100 Hz	18 dB/octave	-6 dB/octave
Ph4	200 Hz	18 dB/octave	-6 dB/octave
Ph5	400 Hz	18 dB/octave	-6 dB/octave
Ph6	Auditory bandA	12 dB/octave	-6 dB/octave

Output impedance at all
outputs

1 , unsymmetrical

Max load at outputs

1 mA, short circuit proof

Power

± 19 V, ± 35 mA

Dimensions

Height 177 mm (7")
Width 54.5 mm (1/8 module)
Depth 200 mm
Weight 800 g

APPENDIX 1 (cont'd); Technical Data for Nihon-Khoden PCG-Pulse
Amplifier AG - 531D.

A Apexcardiogram Measurement;

Transducer Used	ACG/PCG transducer, TK-211S
Maximum Sensitivity	25 times or greater
Time Constant	3 seconds, $\pm 30\%$ In READY mode operation; 0.1sec, $\pm 30\%$
High Frequency Region Characteristics	At 200Hz, -3dB or better, referred to 10Hz
Sensitivity Control	a) Continuous Control; 40dB, within ± 3 dB b) X10(JVP); 10 times, within $\pm 20\%$
Internal Noise Level	1mV peak-to-peak, referred to input, Cg = 2,000pF

B Phonocardiogram Measurement;

Transducer Used	ACG/PCG transducer, TK-211S
Equalizer and Filter Characteristics	Overall characteristics are as shown in Fig.1 Cg = 2,000pF, error; ± 3 dB or less
Filters and Maximum Sensitivity	Filter "L"; 50dB or greater, at 300Hz Filter "M ₁ "; 52dB or greater, at 300Hz
Sensitivity Control	Continuously variable from maximum to zero.
Internal Noise Level	60uV peak-to-peak, referred to input at the filter "M ₁ " and maximum
Mutual Interference between Channels	-40dB or less, an output signal amplitude ratio leaked on an adjacent channels(s) when an input signal of 100Hz, 0.2V peak-to- peak is applied to one of the channels to produce a 10mV output voltage.

APPENDIX 2.1

ST1 Values for Anaesthetised, Normal Dogs

APPENDIX 2.1:

HR	QS ₂	PEP	LVET	Q-C	SUT	PEP/LVET	HR	QS ₂	PEP	LVET	Q-C	SUT	PEP/LVET
175	210	64.8	145.2	30.0	34.8	0.45	140	252	78.0	174.0	36.0	42.0	0.45
175	222	68.0	154.4	30.0	38.0	0.44	135	252	82.0	170.0	36.0	46.0	0.48
153	243	69.2	174.0	26.0	43.2	0.40	133	260	77.6	182.4	36.0	41.6	0.43
153	242	71.2	170.4	28.0	43.2	0.42	152	240	64.0	176.0	32.0	32.0	0.36
153	241	68.4	172.4	28.4	40.0	0.40	133	252	76.0	176.0	31.6	44.4	0.43
157	232	62.4	169.6	26.0	36.4	0.37	133	249	73.2	176.0	32.0	41.2	0.42
144	256	69.6	186.4	30.0	39.6	0.37	117	280	74.4	205.6	32.0	42.4	0.36
144	258	70.4	187.6	30.0	40.4	0.38	128	269	71.6	197.2	30.0	41.6	0.36
106	284	82.0	202.0	30.0	52.0	0.41	118	268	73.2	194.8	28.0	45.2	0.38
107	286	85.6	200.8	31.2	54.4	0.43	118	268	74.0	194.0	28.0	46.0	0.38
107	291	93.0	198.0	40.0	53.0	0.47	118	269	73.2	196.8	26.8	46.4	0.37
104	289	87.2	202.4	30.8	56.4	0.43	118	270	73.2	195.6	28.0	45.2	0.37
142	257	76.0	180.8	30.0	46.0	0.42	125	264	76.0	188.0	32.0	44.0	0.40
140	260	76.0	184.0	30.0	46.0	0.41	126	261	76.0	184.4	32.0	44.0	0.41
139	263	72.0	190.8	30.0	42.0	0.38	125	260	73.6	186.4	32.0	41.6	0.39
110	277	71.2	206.0	28.0	43.2	0.35	126	263	74.0	189.2	32.0	42.0	0.39
117	273	72.0	201.2	28.0	44.0	0.36	126	264	74.0	190.0	32.0	42.0	0.40
113	276	79.2	196.8	28.0	51.2	0.40	131	272	76.0	196.0	34.0	42.0	0.39
109	277	70.0	207.2	28.0	42.0	0.34	130	272	76.0	196.0	34.0	42.0	0.39
119	267	77.2	190.0	32.0	45.2	0.41	128	275	77.2	198.0	34.0	43.2	0.40
118	266	80.4	186.0	32.0	48.4	0.43	103	278	82.0	196.0	30.0	52.0	0.42
118	268	74.8	193.2	32.0	42.8	0.39	99	282	72.4	209.2	30.0	42.4	0.35
119	268	82.0	186.0	32.0	50.0	0.44	101	280	69.2	211.2	30.0	39.2	0.33
125	264	76.0	188.0	32.0	44.0	0.40	99	283	82.8	200.0	31.2	51.6	0.41
125	264	72.0	192.0	29.2	42.8	0.38	121	256	81.6	174.4	32.8	48.8	0.47
127	266	72.0	194.0	34.0	38.0	0.37	121	256	79.6	176.4	32.0	47.6	0.45
128	267	71.2	196.0	30.0	41.2	0.36	121	256	80.0	176.0	32.0	48.0	0.45
135	258	74.0	184.0	30.0	44.0	0.40	131	260	72.8	186.8	28.0	44.8	0.39
134	256	74.0	182.0	28.8	45.2	0.41	128	260	74.4	185.6	28.0	46.4	0.40
135	258	74.4	183.6	30.0	44.4	0.41	126	261	72.4	188.4	28.4	44.4	0.38
134	260	74.0	185.6	30.0	44.0	0.40	131	260	74.0	186.0	28.0	46.0	0.40

APPENDIX 2.1:

HR	QS ₂	PEP	LVET	Q-C	SUT	PEP/LVET
140	261	70.0	191.0	30.0	40.0	0.37
126	272	74.4	197.6	32.0	42.4	0.38
120	275	80.4	194.8	30.4	50.0	0.41
119	276	73.6	202.4	30.0	43.6	0.36
125	260	68.0	191.6	28.0	40.0	0.35
121	260	70.0	190.4	28.0	42.0	0.37
130	256	66.8	189.2	28.0	38.8	0.35
122	268	68.0	200.0	24.0	44.0	0.34
122	268	67.6	200.4	24.0	43.6	0.34
121	270	78.0	192.0	30.4	47.6	0.41
118	272	77.2	195.2	32.8	44.4	0.40
116	276	76.0	200.0	31.0	42.0	0.38
114	274	72.8	201.6	27.0	42.8	0.31
114	276	74.4	201.6	27.6	46.4	0.37
121	272	73.2	198.8	30.0	43.2	0.37
121	273	73.6	199.2	30.0	43.6	0.37
121	272	72.8	199.2	30.0	42.8	0.37
121	276	74.0	202.0	30.0	44.0	0.37
123	256	73.6	182.4	29.6	44.4	0.40
103	274	68.8	205.6	28.0	40.8	0.33
98	276	67.2	208.8	27.6	50.0	0.32
98	290	72.8	217.6	28.0	48.0	0.33
101	288	68.0	220.4	28.0	40.0	0.31
99	290	72.8	216.0	28.8	44.0	0.34
125	264	71.5	192.5	29.5	42.0	0.37
125	260	70.8	189.2	27.6	43.2	0.37
125	264	75.6	188.4	29.6	46.0	0.40
127	260	70.8	189.2	27.6	43.2	0.37
126	264	74.0	190.0	26.0	48.0	0.39
125	263	72.4	190.8	26.4	46.0	0.38
123	266	76.0	190.4	26.0	50.0	0.40

APPENDIX 2.2

ST1 Values from Anaesthetised Dogs

three months after LAD coronary artery ligation

APPENDIX 2.2:

HR	QS2	PEP	LVET	Q-C	SUT	PEP/LVET	HR	QS2	PEP	LVET	Q-C	SUT	PEP/LVET
127	249	74.8	174.0	43.2	31.6	0.43	98	268	82.8	185.2	34.0	48.8	0.45
124	252	72.8	177.2	40.0	32.8	0.41	104	260	58.0	202.0	28.0	30.0	0.29
124	248	69.2	178.8	40.0	29.2	0.39	109	256	67.2	188.8	28.0	39.2	0.36
126	248	71.2	176.8	40.0	31.2	0.40	135	256	72.0	183.6	34.0	38.0	0.39
146	228	76.0	152.0	34.0	42.0	0.50	137	248	76.0	172.0	34.0	42.0	0.44
148	230	68.0	161.6	32.0	36.0	0.42	128	256	74.0	182.4	33.2	40.8	0.41
148	228	66.0	162.0	28.0	38.0	0.41	136	258	75.2	182.8	34.0	41.2	0.41
146	227	78.8	148.0	34.0	44.8	0.53	137	236	71.6	164.4	29.6	42.0	0.44
150	224	67.6	156.4	27.6	40.0	0.43	130	244	68.0	175.6	28.0	40.0	0.39
180	218	61.6	156.0	28.0	33.6	0.39	128	244	68.4	175.6	28.4	40.0	0.40
149	232	70.0	162.4	30.0	40.0	0.43	128	244	72.0	172.0	30.0	42.0	0.42
149	236	68.0	168.0	30.0	38.0	0.40	127	252	74.4	177.6	32.0	42.4	0.42
149	235	66.0	169.2	30.0	36.0	0.39	124	254	72.4	181.2	32.4	40.0	0.40
149	240	72.0	168.0	32.0	40.0	0.43	122	256	60.8	195.2	29.2	31.6	0.31
136	244	70.0	174.0	32.0	38.0	0.40	118	260	80.0	180.0	34.0	46.0	0.44
136	244	70.0	174.0	32.0	38.0	0.40	130	256	60.8	195.2	28.0	32.8	0.31
136	246	70.0	176.0	32.0	38.0	0.40	123	258	60.8	197.2	28.0	32.8	0.31
159	223	56.8	164.0	30.4	26.4	0.34	128	240	70.2	169.8	39.2	30.8	0.41
159	220	60.8	159.2	30.8	30.0	0.38	123	258	54.4	204.0	39.2	30.4	0.27
159	223	69.6	150.4	44.0	25.6	0.46	121	257	54.0	202.8	40.0	38.0	0.27
148	240	60.0	180.0	32.0	28.0	0.33	113	272	53.6	218.4	23.6	30.0	0.25
144	240	64.0	176.0	32.0	32.0	0.36	112	276	50.0	225.6	29.6	20.4	0.22
142	243	63.6	179.6	35.2	28.4	0.35	118	260	79.2	180.8	40.0	39.2	0.44
140	246	63.2	183.2	35.2	28.0	0.34	116	269	71.2	197.6	38.8	32.4	0.36
142	254	90.8	163.6	36.0	54.8	0.56	126	257	69.2	187.6	37.6	31.6	0.37
139	256	63.6	192.4	26.8	36.8	0.33	121	253	78.0	174.8	32.0	46.0	0.45
136	255	72.0	183.2	29.2	42.8	0.39	121	254	78.4	175.6	34.0	44.4	0.45
110	280	85.6	194.4	30.0	55.6	0.44	121	256	80.4	175.6	32.0	48.4	0.46
99	291	92.0	198.6	37.2	54.8	0.46	142	233	59.6	173.6	20.0	39.6	0.34
99	268	86.4	181.6	32.4	54.0	0.48	146	232	56.0	176.2	20.0	36.0	0.32

APPENDIX 2.2:

<u>HR</u>	<u>QS₂</u>	<u>PEP</u>	<u>LVET</u>	<u>Q-C</u>	<u>SUT</u>	<u>PEP/LVET</u>
118	242	64.0	177.6	28.0	36.0	0.36
128	232	61.2	170.4	25.2	36.0	0.36
134	232	64.8	166.8	27.2	37.6	0.39
134	233	64.0	168.8	26.0	38.0	0.38
133	231	63.6	167.6	28.0	35.6	0.38
130	228	64.0	164.0	32.0	32.0	0.39
133	228	70.0	158.0	30.0	40.0	0.44
111	266	64.0	202.0	26.0	38.0	0.32
153	220	51.6	168.4	25.6	26.0	0.31
152	226	59.2	166.4	26.0	33.2	0.36
148	224	58.8	165.2	26.0	32.8	0.36

APPENDIX 2.3 (a)

ST1 Values from Conscious, Normal Dogs

APPENDIX 2.3 (b)

ST1 Values for Appendix 2.3 (a) Dogs

(Anaesthetised for comparison)

APPENDIX 2.3 (a)

HR	QS ₂	PEP	LVET	Q-C	SUT	PEP/LVET	HR	QS ₂	PEP	LVET	Q-C	SUT	PEP/LVET
82	239	47.6	191.6	28.8	18.8	0.25	109	236	49.6	186.0	20.0	29.6	0.27
82	240	54.4	185.6	26.4	28.0	0.29	109	235	49.6	185.2	18.4	31.2	0.27
107	236	44.0	192.4	23.6	20.4	0.23	117	231	49.6	181.6	18.4	38.4	0.27
88	249	48.8	200	26.0	22.8	0.24	112	233	62.0	171.2	19.6	42.4	0.36
87	258	63.2	194.4	40.0	23.2	0.33	79	243	55.6	187.6	18.0	37.6	0.30
88	258	54.0	203.6	32.0	22.0	0.27	180	173	46.4	126.4	19.2	27.2	0.37
90	256	54.0	202.0	32.8	21.2	0.27	144	230	60.4	170.0	22.4	38.0	0.36
80	245	42.4	202.4	28.0	14.4	0.21	115	245	60.8	184.0	22.8	38.0	0.33
120	226	38.4	188.0	20.0	18.4	0.20	134	223	58.0	165.2	20.4	37.6	0.35
101	242	45.6	196.8	25.6	20.0	0.23	115	236	44.8	191.2	12.0	32.8	0.23
82	258	45.2	213.2	29.2	16.0	0.21	126	236	46.8	189.6	14.0	32.8	0.25
77	252	46.0	206.0	26.0	20.0	0.22	117	236	47.2	188.4	12.0	35.2	0.25
82	253	50.4	202.8	41.2	9.2	0.25	113	248	57.2	190.4	21.2	36.0	0.30
88	260	55.6	204.4	29.6	26.0	0.27	101	235	50.8	184.0	23.6	27.2	0.28
88	258	51.0	207.4	28.0	23.0	0.25	120	221	48.4	172.4	24.4	24.0	0.28
88	258	56.0	202.0	36.4	19.6	0.28	112	226	62.8	162.8	24.0	38.8	0.39
102	237	47.6	189.2	35.2	12.4	0.25	92	253	62.8	190.4	24.0	37.2	0.33
118	237	52.4	184.4	26.4	26.0	0.28	102	247	60.4	186.8	22.8	37.6	0.32
88	242	44.8	196.8	24.4	20.4	0.23	188	164	36.8	126.8	10.0	26.8	0.29
90	242	52.4	189.2	26.0	24.4	0.28	200	159	50.4	108.8	19.2	31.2	0.46
77	245	50.4	194.8	26.4	24.0	0.26	210	149	50.4	89.8	22.4	28.0	0.57
87	270	53.0	217.0	18.0	35.0	0.24	155	200	65.0	135.0	30.0	35.0	0.48
91	270	50.0	220.0	20.0	30.0	0.23	152	205	52.4	152.4	22.4	30.0	0.34
94	260	55.0	205.0	25.0	30.0	0.27	134	227	54.8	172.4	20.8	34.0	0.32
111	250	60.0	190.0	25.0	35.0	0.32	111	230	52.4	177.2	20.4	32.0	0.30
104	250	60.0	190.0	25.0	35.0	0.32	115	222	51.2	170.8	20.4	30.8	0.30
99	255	60.0	195.0	25.0	35.0	0.31	124	214	49.2	164.4	10.0	39.2	0.30
101	260	60.0	200.0	25.0	35.0	0.30	88	233	57.6	176.0	22.0	35.6	0.33
100	250	60.0	190.0	20.0	40.0	0.32	115	234	57.2	177.2	22.8	34.4	0.32
115	217	51.6	165.6	21.2	30.4	0.31	92	240	52.4	187.2	20.4	32.0	0.28
							129	220	52.4	168.4	20.0	32.4	0.31

APPENDIX 2.3 (a)

<u>HR</u>	<u>QS₂</u>	<u>PEP</u>	<u>LVET</u>	<u>Q-C</u>	<u>SUT</u>	<u>PEP/LVET</u>
200	174	50.8	122.8	21.2	29.6	0.41
145	198	50.0	148.0	20.4	29.6	0.34
110	220	58.4	161.6	26.4	32.0	0.36
110	210	60.0	150.0	29.0	31.0	0.40
96	215	58.4	156.6	24.4	34.0	0.37
99	226	53.6	172.8	20.0	33.6	0.31
104	213	54.8	158.4	21.3	33.2	0.35
109	212	56.0	156.0	20.0	36.0	0.36
117	230	60.0	169.6	24.0	36.0	0.35
88	236	46.4	189.6	18.4	28.0	0.24
120	208	52.8	154.4	21.2	31.6	0.34

APPENDIX 2.3 (b)

HR	QS ₂	PEP	L _{VET}	Q-C	SUT	PEP/L _{VET}	HR	QS ₂	PEP	L _{VET}	Q-C	SUT	PEP/L _{VET}
85	273	66.0	206.8	24.0	42	0.32	76	270	69.2	201.2	21.2	48.0	0.34
81	275	76.4	198.4	26.0	50.4	0.39	104	268	69.2	198.8	24.0	45.2	0.35
88	276	72.0	203.6	23.2	48.8	0.35	102	274	72.8	201.2	22.8	50.0	0.36
134	242	64.4	178.0	16.8	47.6	0.36	101	272	74.0	198.0	24.8	49.2	0.37
128	240	61.6	178.0	19.2	42.4	0.35	121	232	62.8	168.8	28.8	34.0	0.37
71	282	58.4	224.0	23.2	35.2	0.26	121	240	58.0	182.0	28.0	30.0	0.32
63	284	64.4	220.0	20.4	44.0	0.29	118	240	58.0	182.0	28.0	30.0	0.32
63	284	72.8	211.2	22.8	50.0	0.34	175	210	64.8	145.2	30.0	34.8	0.45
65	280	61.2	218.8	20.4	40.8	0.28	175	222	68.0	154.4	30.0	38.0	0.44
133	244	57.6	186.4	19.6	38.0	0.31	153	243	69.2	173.6	26.0	43.2	0.40
132	245	57.6	187.6	20.0	37.6	0.31	153	242	71.2	170.4	28.0	43.2	0.42
134	240	54.2	176.0	19.6	44.6	0.36	153	241	68.4	172.4	28.4	40.0	0.40
131	242	62.8	179.6	20.0	42.8	0.35	155	232	62.4	169.6	26.0	36.4	0.37
75	272	74.0	198.0	26.0	48.0	0.37	130	244	65.2	178.4	28.4	36.8	0.37
79	276	76.0	199.6	24.8	51.2	0.38	124	245	68.0	176.8	28.0	40.0	0.39
79	276	80.0	196.0	26.4	53.6	0.41	133	260	77.6	182.4	36.0	41.6	0.43
80	280	79.6	200.4	26.4	53.2	0.40	152	240	64.0	176.0	32.0	32.0	0.36
141	224	63.2	160.4	24.0	39.2	0.39	126	272	74.4	197.6	32.0	42.4	0.38
137	225	61.6	163.6	20.8	40.8	0.38	120	275	80.4	194.8	30.4	50.0	0.41
136	227	62.4	164.8	21.6	40.8	0.38	119	276	73.6	202.4	30.0	43.6	0.36
100	272	58.8	213.6	20.0	38.8	0.28	125	260	68.0	191.6	28.0	40.0	0.35
98	273	64.0	208.8	22.0	42.0	0.31	121	260	70.0	190.4	28.0	42.0	0.37
103	259	61.6	197.2	22.0	39.6	0.31	130	256	66.8	189.2	28.0	38.8	0.35
95	266	64.4	201.6	22.8	41.6	0.32	122	268	68.0	200.0	24.0	44.0	0.34
132	262	70.4	191.6	24.0	46.4	0.37	122	268	67.6	200.4	24.0	43.6	0.34
140	264	70.0	194.0	20.0	50.0	0.36	121	270	78.0	192.0	30.4	47.6	0.41
115	269	72.0	197.2	22.0	50.0	0.37	117	272	77.2	195.2	32.8	44.4	0.40
82	272	71.2	200.8	21.2	50.0	0.35	116	276	76.0	200.0	34.0	42.0	0.38
88	268	71.2	197.8	21.2	50.0	0.36	114	274	72.8	201.6	30.0	42.8	0.31
77	265	65.6	199.6	20.0	45.6	0.33	114	276	74.4	201.6	28.0	46.4	0.37

APPENDIX 2.4:

STI Values from Dogs with Clinical or Suspected Heart Disease

APPENDIX 2.4:

HR	QS2	PEP	LVET	Q-C	SUT	PEP/LVET	HR	QS2	PEP	LVET	Q-C	SUT	PEP/LVET
151	197	67.0	130.0	26.7	40.0	0.51	115	221	100.0	121.4	40.0	60.0	0.82
150	197	70.0	127.0	30.0	40.0	0.55	115	230	73.4	156.6	33.4	40.0	0.47
107	210	80.0	118.3	31.7	48.3	0.68	89	217	58.3	158.3	25.0	33.3	0.37
136	205	53.3	151.6	21.6	31.6	0.35	151	217	53.3	163.4	18.3	35.0	0.66
131	207	41.6	158.3	16.6	23.3	0.26	172	218	65.0	153.3	25.0	40.0	0.42
116	217	46.6	170.0	20.0	26.3	0.27	172	211	65.0	145.6	25.0	40.0	0.45
165	175	41.6	131.6	20.0	21.6	0.32	155	198	49.9	148.4	28.3	21.6	0.35
169	182	45.0	135.0	21.6	23.3	0.33	111	243	81.2	162.4	30.0	51.2	0.50
153	197	50.0	146.6	23.3	26.6	0.34	115	237	75.0	161.6	30.0	45.0	0.46
140	197	90.0	103.3	25.0	65.0	0.87	120	227	65.0	161.6	25.0	40.0	0.40
155	187	55.0	133.3	21.6	31.6	0.41	149	208	49.4	158.9	19.4	30.0	0.31
170	185	55.0	130.0	23.3	31.6	0.42	153	218	54.9	163.5	18.3	36.6	0.34
60	220	85.0	135.0	35.0	50.0	0.63	176	170	51.3	118.7	21.3	30.0	0.43
77	260	65.0	195.0	28.3	36.6	0.33	158	190	55.0	135.0	25.0	30.0	0.41
78	260	62.0	198.4	25.0	36.6	0.31	166	180	55.0	125.0	25.0	30.0	0.44
213	171	37.7	133.5	11.3	26.6	0.28	149	211	98.4	113.0	38.4	60.0	0.87
189	180	53.2	126.7	15.0	38.3	0.42	192	167	45.0	121.7	20.0	25.0	0.37
160	223	60.0	163.3	30.0	30.0	0.37	153	183	64.8	118.4	23.2	41.6	0.55
178	250	75.0	175.0	25.0	50.0	0.43	159	177	66.6	110.0	26.6	40.0	0.61
156	230	70.0	160.0	25.0	45.0	0.44	172	178	60.0	118.3	20.0	40.0	0.51
105	267	85.0	181.6	45.0	40.0	0.47	136	230	60.0	170	25.0	35.0	0.35
220	190	70.0	120.0	35.0	35.0	0.58	134	211	63.2	148.1	26.6	36.6	0.43
87	248	68.2	180.0	30.0	38.2	0.38	170	227	67.9	158.7	21.3	46.6	0.43
136	252	69.9	181.7	33.3	36.6	0.38	176	228	69.8	158.5	26.4	43.4	0.44
77	263	73.3	190.0	33.3	40.0	0.39	86	240	58.3	181.7	28.3	30.0	0.32
68	242	66.6	175.0	26.6	40.0	0.38	211	193	53.4	140.0	20.0	33.4	0.38
161	198	45.0	153.3	20.0	25.0	0.29	88	238	66.6	171.8	26.6	40.0	0.39
86	250	75.0	175.0	25.0	50.0	0.43	91	250	63.4	186.6	25.0	38.4	0.34
91	245	80.0	165.0	35.0	45.0	0.48	94	245	61.7	183.3	28.4	33.3	0.34
115	233	81.3	152.0	31.3	50.0	0.53	88	237	78.3	158.3	28.3	50.0	0.49

APPENDIX 2.4:

<u>HR</u>	<u>QS₂</u>	<u>PEP</u>	<u>LVET</u>	<u>Q-C</u>	<u>SUT</u>	<u>PEP/LVET</u>
115	288	78.1	159.9	30.0	48.1	0.49
84	212	65.8	145.8	26.6	38.2	0.45
78	217	68.2	148.5	23.2	45.0	0.46
72	208	66.2	142.2	25.0	41.2	0.47
130	205	58.2	146.8	30.0	28.2	0.40
128	208	58.2	150.1	30.0	28.2	0.39
211	180	38.3	141.7	15.0	23.3	0.27
197	180	45.0	135.0	25.0	20.0	0.33
89	231	55.0	176.4	20.0	35.0	0.31
87	220	56.4	163.6	23.2	33.2	0.34
90	240	55.0	185.0	20.0	35.0	0.30

APPENDIX 3:

Computer Programs

>> Program for STI calculation

```

1  REM SYSTOLIC TIME INTERVAL CALCULATION ROUTINE FOR F.M.KYDD MARCH 1982
9  ON ERROR GOTO 1080
10 DIM D$(8) : D$="#####.#"
20 K$="#####.#"
30 INPUT"NUMBER OF VALUES TO BE MEANED= ",A
40 INPUT" MULTIPLICATION FACTOR= ",B
60 C=1 : I=1
70 DIM Q(7,6),C(7,6),S(7,6),T(7,6),P(7,6),A(7,6),A1(7,6),I(7,6)
80 REM Q=QS2,C=Q-C,S=SUT,T=T-PEAK,P=Q-PEAK,A=dA/dt,A1=da/dt,A-1
90 K=I(J,M)
100 INPUT" QS2= ",Q(I,G)
105 @G
110 INPUT" Q-C= ",C(I,G)
120 INPUT" SUT= ",S(I,G)
130 INPUT" T-Peak=",T(I,G)
140 INPUT" Q-Peak=",P(I,G)
150 INPUT" dA/dt= ",A(I,G)
160 INPUT"dA/dt,A-1= ",A1(I,G)
215 REM KEEP RUNNING TOTAL OF QS2^^^^^^^^^Q1
220 Q1=Q1+(Q(I,G)*B)
225 REM KEEP RUNNING TOTAL OF Q-C^^^^^^^^^D1
230 D1=D1+(C(I,G)*B)
235 REM RUNNING TOTAL OF SUT^^^^^^^^^S1
240 S1=S1+(S(I,G)*B)
245 REM RUNNING TOTAL OF T-PEAK^^^^^^T1
250 T1=T1+(T(I,G)*B)
255 REM RUNNING TOTAL OF Q-PEAK^^^^^^P1
260 P1=P1+(P(I,G)*B)
265 REM RUNNING TOTAL OF dA/dt^^^^^^^^^H1
270 H1=H1+A(I,G)
275 REM RUNNING TOTAL OF dA/dt,A-1^^^^^^O1
280 O1=O1+(A1(I,G))
305 @
315 REM RUNNING TOTAL OF QS2 SQUARED^^^^^^^^^Q2
320 Q2=Q2+(Q(I,G)*B)*(Q(I,G)*B)
325 REM RUNNING TOTAL OF Q-C SQUARED^^^^^^^^^D2
330 D2=D2+((C(I,G)*B)*(C(I,G)*B))
335 REM RUNNING TOTAL OF SUT SQUARED^^^^^^^^^S2
340 S2=S2+((S(I,G)*B)*(S(I,G)*B))
345 REM RUNNING TOTAL OF T- PEAK SQUARED
350 T2=T2+((T(I,G)*B)*(T(I,G)*B))
355 REM RUNNING TOTAL OF Q-PEAK SQUARED^^^^^^P2
360 P2=P2+((P(I,G)*B)*(P(I,G)*B))
365 REM RUNNING TOTAL OF dA/dt^^^^^^^^^H2
370 H2=H2+(A(I,G)*A(I,G))
375 REM RUNNING TOTAL OF dA/dt,A-1^^^^^^O2
380 O2=O2+(A1(I,G)*A1(I,G))
385 IF G=A THEN GOTO 400
390 G=G+1
395 GOTO 100
400 REM MEAN VALUE CALCULATION ROUTINE
405 REM MEAN QS2=Q3
410 Q3=Q1/A
415 REM MEAN Q-C=D3
420 D3=D1/A
425 REM MEAN SUT=S3
430 S3=S1/A
435 REM MEAN T-PEAK=T3
440 T3=T1/A
445 REM Q-PEAK =P3
450 P3=P1/A

```

```

455 REM MEAN dA/dt=H3
460 H3=H1/A
465 REM MEAN dA/dt.A-1=O3
470 O3=O1/A
510 Z1=(Q1*Q1)/A : Z2=(D1*D1)/A : Z3=(S1*S1)/A : Z4=(T1*T1)/A : Z5=(P1*P1)/A
515 Z6=(H1*H1)/A : Z7=(O1*O1)/A
520 U1=Q2-Z1 : U2=D2-Z2 : U3=S2-Z3 : U4=T2-Z4 : U5=P2-Z5 : U6=H2-Z6 : U7=O2-Z7
530 F=A-1
540 W1=U1/F : W2=U2/F : W3=U3/F : W4=U4/F : W5=U5/F : W6=U6/F : W7=U7/F
545 R1=SQR(W1) : R2=SQR(W2) : R3=SQR(W3) : R4=SQR(W4) : R5=SQR(W5) : R6=SQR(W6) : R7=SQR(W7)
546 R7=SQR(W7)
560 REM R1=STD DEV.
565 X=SQR(A)
570 X1=R1/X : X2=R2/X : X3=R3/X : X4=R4/X : X5=R5/X : X6=R6/X : X7=R7/X
580 REM X=STD.ERROR
590 @ "QS2 MEAN=" , Q3
600 @ "QS2 STD.DEV.=" , R1
610 @ "QS2 STD.ERROR=" , X
620 OPEN \3\ "LP"
630 @ \3\
640 I=1 : G=1
650 @ \3\ " QS2=" , Q(I,G)
660 @ \3\ " Q-C=" , C(I,G)
670 @ \3\ " SUT=" , S(I,G)
680 @ \3\ " T-peak=" , T(I,G)
690 @ \3\ " Q-peak=" , P(I,G)
700 @ \3\ " dA/dt=" , A(I,G)
710 @ \3\ " dA/dt.A-1=" , A1(I,G)
715 @ \3\
716 @ \3\
720 IF G=A THEN GOTO 740
725 G=G+1
730 GOTO 650
740 @ \3\
750 @ \3\
760 @ \3\ "QS2 MEAN =" , Q3
770 @ \3\ " QS2 STD.DEV =" , R1
780 @ \3\ " QS2 STD.ERR. =" , X1
790 @ \3\
800 @ \3\ "Q-C MEAN =" , D3
810 @ \3\ " Q-C STD.DEV =" , R2
820 @ \3\ " Q-C =" , X2
830 @ \3\
840 @ \3\
850 @ \3\ " SUT MEAN =" , S3
860 @ \3\ " SUT STD.DEV =" , R3
870 @ \3\ "SUT STD.ERR. =" , X3
880 @ \3\
890 @ \3\
900 @ \3\ " T-peak MEAN =" , T3
910 @ \3\ " T-peak STD.DEV. =" , R4
920 @ \3\ " T-peak STD.ERR. =" , X4
930 @ \3\
940 @ \3\
950 @ \3\ " Q-peak MEAN =" , P3
960 @ \3\ " Q-peak STD.DEV =" , R5
970 @ \3\ " Q-peak STD.ERR. =" , X5
980 @ \3\
990 @ \3\
1000 @ \3\ "dA/dt mean =" , H3
1010 @ \3\ " dA/dt STD.DEV. =" , R6
1020 @ \3\ "dA/dt STD.DEV=" , X6
1030 @ \3\

```

```
1040 @\3\  
1050 @\3\" dA/dt,A-1 =",O3  
1060 @\3\"dA/dt,A-1 STD.DEV.=",R7  
1070 @\3\" dA/dt,A-1=",X7  
1075 @\3\  
1076 @\3\  
1080 CLOSE\3\  
1090 @  
1100 INPUT"ANALYSE ANY MORE DATA ?",Z$  
1110 IF Z$="YES"THEN GOTO 1160  
1120 IF Z$="NO"THEN GOTO 1140  
1125 @" ANSWER THE QUESTION FREDAAAA!!!"  
1130 GOTO 1100  
1140 STOP  
1150 @  
1160 GOTO 10  
1170 STOP
```

Sum, Square & Correlation Calculation

Line 899 - 2020

```

899 BORDER 1: PAPER 1: INK 7
900 CLS : PRINT "TAB 3;"ENTER
910 PRINT "TAB 4;"1) ENTER VA
LUES";TAB 4;"2) PRINT VALUES";TA
B 4;"3) EXAMINE/CORRECT ENTRIES";
TAB 4;"4) SAVE PROGRAM";TAB 4;"
5) INITIALISE";TAB 4;"6) STOP WO
RK"
920 IF INKEY$<>"" THEN GO TO 92
930 LET B$=INKEY$: IF B$="" THE
N GO TO 930
950 IF B$="1" THEN CLS : GO TO
1000
955 IF B$="2" THEN CLS : GO TO
2000
960 IF B$="3" THEN CLS : GO TO
4000
965 IF B$="4" THEN CLS : GO TO
5000
970 IF B$="5" THEN CLS : GO TO
6000
975 IF B$="6" THEN CLS : GO TO
7000
980 GO TO 920
1000 LET X=5: PRINT AT 0,0;"ENTE
R VALUES";AT 0,10;"ENTRIES: ";N;
AT 1,0;"(-9999 to quit)";AT 3,0;
"X value";AT 3,10;"Y value"
1010 LET N=N+1: LET X=X+1
1020 INPUT "X value ";b: IF b=-9
999 THEN LET N=N-1: GO TO 900
1040 LET a(1,N,1)=b: PRINT AT X,
3;b
1045 LET t(1)=t(1)+b
1050 LET a(1,N,3)=b*b
1055 LET t(3)=t(3)+(b*b)
1060 INPUT "Y value ";b
1062 IF b=-9999 THEN BEEP .1,20:
GO TO 1050
1070 LET a(1,N,2)=b: PRINT AT X,
10;b
1075 LET t(2)=t(2)+b
1080 LET a(1,N,4)=b*b: LET a(1,N
,5)=a(1,N,1)*a(1,N,2)
1085 LET t(4)=t(4)+(b*b): LET t(
5)=t(5)+a(1,N,5)
1090 LET b=a(1,N,5): LET a(1,N,6
)=b*b
1095 LET t(6)=t(6)+a(1,N,6)
1100 IF X=21 THEN LET X=4: FOR i
=5 TO 21: PRINT AT i,0);... NEXT
i
1110 PRINT AT 0,20;n
1120 IF N=0 THEN PRINT AT 0,0; F
LASH 1;"FILE FULL"; FLASH 0;...:
PAUSE 300: GO TO 900
1130 GO TO 1010
2000 PRINT TAB 12;"TOTALS"
2010 GO SUB 2200
2020 PRINT AT 3,0;"X" = "t(1
)";AT 4,0;"Y" = "t(2)";AT 5,0;
"X^2" = "t(3)";AT 6,0;"Y^2" =
"t(4)";AT 7,0;"X*Y" = "t(5)";AT
8,0;"X*Y^2" = "t(6)";

```

Line 2080 - 4190

```

2080 PRINT AT 10,10;"COMPUTATION
S"
2090 PRINT AT 12,0;"A";TAB 6;"="
TAB 8;ANS1;TAB 0;"B";TAB 6;"="
TAB 8;ANS2;TAB 0;"C";TAB 6;"="
TAB 8;ANS3;TAB 0;"D";TAB 6;"="
TAB 8;ANS4;TAB 0;"E";TAB 6;"="
TAB 8;ANS5
2100 PRINT AT 20,0;"PRESS A KEY
TO RETURN TO MENU"
2110 PAUSE 0: GO TO 900
2200 LET ANS1=T(3)-((T(1)+T(1))/
N)
2210 LET ANS2=T(4)-((T(2)+T(2))/
N)
2220 LET ANS3=T(5)-((T(1)+T(2))/
N)
2230 LET ANS4=ANS3/(SQR (ANS1*AN
S2))
2240 LET ANS5=(T(6)-(T(5)+T(5)/N
))/N-1
2250 RETURN
3500 STOP
4000 CLS : PRINT "EXAMINE ENTRIE
S"
4010 PRINT ""FROM START (Y/N)"
4015 INPUT "Y/N ";B$
4020 IF B$="Y" OR B$="y" THEN LE
T S=1: LET F=N-1: GO TO 4120
4030 IF B$<>"N" AND B$<>"n" THEN
GO TO 900
4040 CLS : PRINT "FROM WHICH ENT
RY DO YOU WISH TO START?" "" (Las
t entry is No.);n
4050 INPUT "start ";s: IF s>n TH
EN BEEP .1,20: GO TO 4050
4060 PRINT ""ENTER THE AMOUNT
OF ENTRIES YOU WISH TO LOOK AT."
: LET W=N-S
4070 INPUT ("Amount (no. from 1
to ";W;"");f
4075 IF f>W THEN BEEP .1,20: GO
TO 4070
4080 PRINT ""START = ";S;"END
= ";S+F
4100 PRINT ""PRESS C TO CONFIRM
": INPUT C$: IF C$<>"C" AND C$<>
"c" THEN GO TO 4000
4120 FOR J=S TO S+f
4125 CLS : PRINT AT 0,0;"ENTRY "
J
4130 PRINT AT 3,0;"X";TAB 10;A(1
,J,1)
4140 PRINT AT 5,0;"Y";TAB 10;A(1
,J,2)
4150 PRINT AT 7,0;"X^2";TAB 10;A
(1,J,3)
4160 PRINT AT 9,0;"Y^2";TAB 10;A
(1,J,4)
4170 PRINT AT 11,0;"X*Y";TAB 10;
A(1,J,5)
4180 PRINT AT 13,0;"X*Y^2";TAB 1
0;A(1,J,6)
4190 PRINT AT 20,0;"C TO CORRECT
O TO QUIT OR ANY OTHER KEY TO
CONTINUE"

```

Line 4200 - 7020

```

4200 INPUT C$
4210 IF C$<>"C" AND C$<>"c" AND
C$<>"0" AND C$<>"q" THEN GO TO 4
240
4220 IF C$="C" OR C$="c" THEN GO
500 4250: GO TO 4240
4230 GO TO 900
4240 NEXT J
4245 GO TO 900
4250 LET OX=0: LET OY=0
4260 LET OX=A(1,J,1): LET OY=A(1
,J,2)
4270 LET T(1)=T(1)-OX: LET T(3)=
T(3)-(OX*OX)
4280 LET T(2)=T(2)-OY: LET T(4)=
T(4)-(OY*OY)
4290 LET T(5)=T(5)-(OX*OY): LET
T(6)=T(6)-(OX*OY)*(OX*OY)
4300 PRINT AT 20,0;
4310 PRINT AT 18,0;"New value x
"; INPUT b: PRINT b
4320 PRINT AT 20,0;"New value y
"; INPUT c: PRINT c
4330 LET a(1,J,1)=b: LET a(1,J,3
)=b*b
4340 LET a(1,J,2)=c: LET a(1,J,4
)=c*c
4350 LET a(1,J,5)=b*c: LET a(1,J
,6)=(b*c)*(b*c)
4360 LET t(1)=t(1)+b: LET t(2)=t
(2)+c
4370 LET t(3)=t(3)+a(1,J,3): LET
t(4)=t(4)+a(1,J,4)
4380 LET t(5)=t(5)+a(1,J,5)
4390 LET t(6)=t(6)+a(1,J,5)*a(1
,J,5)
4400 RETURN
5000 CLS: PRINT "PULL OUT EAR P
LUG"
5010 SAVE "VET1" LINE 899
5050 CLS: PRINT "REWIND TAPE"
INSERT EAR PLUG"; "VERIFYING
": VERIFY "VET1"
5060 GO TO 900
5999 STOP
6000 PRINT "ENTER NUMBER OF ENTR
IES YOU WISHTO MAKE"
6010 INPUT "No. of entries? ";d
6020 PRINT "No. of entries : "
;d
6030 PRINT "Press C to Confirm
": INPUT b$: IF b$="C" OR b$="c
" THEN GO TO 6050
6040 GO TO 900
6050 DIM a(1,d,6): DIM T(6): LET
n=0
6100 GO TO 900
6200 STOP
7000 CLS: PRINT AT 9,4;"TO RE-S
TART - GO TO 900"
7010 PRINT AT 10,4;"-- ----
-- ----"
7020 BEEP .5,20: STOP

```


Linear Regression

```
10 DIM D(100),R(100)
15 ON ERROR GOTO 600
20 DIM D$(30) : D$="###-&&&&.&&&"
30 OPEN\3\"$LP"
100 GOSUB 1000
105 INPUT "NUMBER OF VALUES ",N
110 FOR K=1 TO N
115 INPUT "DOSE",D; : INPUT "RESPONSE",R
120 D(K)=D : R(K)=R
130 X2=X2+(D(K)*D(K))
140 X1=X1+D(K)
150 X=X+(D(K)*R(K))
160 Y1=Y1+R(K)
170 Y2=Y2+(R(K)*R(K))
180 NEXT K
200 REM SLOPE VALUE =B
210 B=(X-((X1*Y1)/N))/((X2-((X1*X1)/N)))
220 REM INTERCEPT VALUE = A
230 A=(Y1/N)-(B*(X1/N))
240 R1=X-(X1*Y1)/N
250 R2=(X2-((X1*X1)/N))*(Y2-((Y1*Y1)/N))
260 R3=R1/SQR(R2)
270 INPUT "DO YOU WISH LINE PRINTER OUTPUT ?",A$
280 IF A$="YES" THEN 400
290 IF A$="NO" THEN 300
300 PRINT "DOSE" RESPONSE "
310 FOR K=1 TO N
320 PRINT D(K); : @SPC(10),R(K)
330 NEXT K
340 PRINT
350 @USING D$,"SLOPE",B; : @USING D$,"INTERCEPT",A; : @USING D$,"R=",R3
360 INPUT "FINISHED ?",B$
370 IF B$="YES" THEN 600
380 IF B$="NO" THEN 500
390 GOTO 360
400 PRINT\3" LINEAR REGRESSION CALCULATION "
405 PRINT\3"DOSE RESPONSE"
410 FOR K=1 TO N
420 PRINT\3\D(K); : @\3\SPC(10),R(K)
440 NEXT K
450 PRINT
460 @\3\USING D$,"SLOPE",B; : @\3\USING D$,"INTERCEPT",A; : @\3\USING D$,"R=",R3
470 INPUT "FINISHED",B$
480 IF B$="YES" THEN 600
490 IF B$="NO" THEN 500
500 X=0 : N=0 : R=0 : D=0 : B=0 : A=0 : R1=0 : R2=0 : R3=0 : Y2=0 : Y1=0
505 X1=0 : X2=0
510 GOTO 100
600 CLOSE\3\
610 STOP
1000 FOR K=0 TO 100
1010 NEXT K
1020 RETURN
```

T-test Estimation

```

10 ON ERROR GOTO 750
20 ON ESC GOTO 750
30 DIM S(100),U(100),D(100)
40 DIM D$(30) : D$="#####&&&&&. &&&&"
50 FOR I=1 TO 5
60 @
70 NEXT I
80 @
90 @
95 OPEN\3\ "$LP"
100 E=0 : E2=0 : D1=0 : D2=0 : Z=0 : Z2=0 : P=0 : P2=0 : T=0 : T2=0 : U=0 :
105 V=0 : N=0 : M=0 : W=0 : W2=0 : G=0 : F=0 : D=0 : X=0 : Y=0 : S2=0 : S=0
110 GOSUB 1090
115 @
116 @
117 INPUT" PARAMETER NAME ".X$
120 INPUT" NUMBER OF VALUES IN SAMPLE 1=",N
125 @
130 INPUT" NUMBER OF VALUES IN SAMPLE 2=",M
135 @
140 FOR K=1 TO N
145 INPUT"FIRST SAMPLE= ".X
155 S(K)=X
160 T=T+S(K)
165 Z=Z+(S(K)*S(K))
170 NEXT K
175 @
180 FOR K=1 TO M
185 INPUT" SECOND SAMPLE",Y
190 U(K)=Y
195 T2=T2+U(K)
200 Z2=Z2+(U(K)*U(K))
205 NEXT K
220 REM P REPRESENTS THE MEAN VALUE OF THE SAMPLE,P2 THE SAME FOR SAMPLE 2
230 P=T/N : P2=T2/M
240 REM D=STANDARD DEVIATION D2= STD DEV FOR SAMPLE TWO
245 S=(T*T)/N
246 U=Z-S
247 F=N-1
248 W=U/F
250 D1=SQR(W)
255 S2=(T2*T2)/M
256 U2=Z2-S2
257 G=M-1
258 W2=U2/G
260 D2=SQR(W2)
270 REM E= STANDARD ERROR OF MEAN WHICH IS STD DEV/SQR N
280 E=D1/SQR(N)
290 E2=D2/SQR(M)
300 REM ANALYSIS OF VARIANCE = DIFFERENCE IN MEANS DIVIDED BY THE SUM
310 REM OF THE SQUARE ROOT OF THE STD'S SQUARED/NUMBER OF VALUES IN THE SAMPL
320 REM R= DIFFERENCE IN THE MEANS
330 R=P-P2
345 REMARK V EQUALS THE ANALYSIS OF VARIANCE T
350 V=R/SQR((D1*D1/N)+(D2*D2/M))
400 INPUT"DO YOU WISH LINE PRINTER LISTING ?",B$
410 IF B$="YES"THEN 590
420 IF B$="NO"THEN 430
425 PRINT X$
430 PRINT" SAMPLE ONE                SAMPLE TWO "
440 FOR K=1 TO N

```

```
450 PRINT S(K); : @SPC(10),U(K)
460 NEXT K
470 PRINT
480 PRINT
500 @USING D$,"SAMPLE MEAN",P; : @SPC(20); : @USING D$,"SAMPLE MEAN",P2
510 @USING D$,"STD DEVIATION",D1; : @SPC(20); : @USING D$,"STD DEVIATION",D2
520 @USING D$,"STD ERROR ",E; : @SPC(20); : @USING D$,"STD ERROR ",E2
530 PRINT
550 @USING D$," t= ",V
555 INPUT" FINISHED ",C$
560 IF C$="YES"THEN 750
565 IF C$="NO"THEN 1040
590 PRINT\3\X$
600 PRINT\3\" SAMPLE ONE      SAMPLE TWO"
601 IF M<N THEN 610
602 IF M>N THEN 604
604 N=M
610 FOR K=1 TO N
620 PRINT\3\S(K); : @\3\SPC(5),U(K)
630 NEXT K
640 @\3\
650 @\3\
665 @\3\USING D$,"SAMPLE MEAN",P; : @\3\SPC(10); : @\3\USING D$,"SAMPLE MEAN
670 @\3\USING D$,"STD DEVIATION",D1; : @\3\SPC(10); : @\3\USING D$,"STD DEVIATION".D
680 @\3\USING D$,"STD ERROR",E; : @\3\SPC(10); : @\3\USING D$,"STD ERROR",E2
690 @\3\
710 @\3\USING D$," t= ",V
715 @\3\
716 @\3\
717 @\3\
720 INPUT"FINISHED ?",A$
730 IF A$="YES"THEN 750
740 IF A$="NO"THEN 1040
750 CLOSE\3\
760 STOP
1040 PRINT
1060 GOTO 100
1080 STOP
1090 FOR K=0 TO 100
1095 D(K)=0 : S(K)=0 : U(K)=0
1100 NEXT K
1110 RETURN
```

APPENDIX 4;

Definitions and Abbreviations

ACG - apexcardiogram
ECG - electrocardiogram
PCG - phonocardiogram

Points of the apexcardiogram

A - atrial component following P wave of the ECG
C - start of the systolic upstroke
E - peak of the ACG
O - nadir of the ACG
RFW - rapid filling wave
SFW - slow filling wave

Intervals of the apexcardiogram

Q-C - electromechanical delay
IVCT - isovolumic contraction time otherwise known as
SUT - systolic upstroke time on C-E
t-dA/dt - time from the onset of rise of the max dA/dt to the peak
Q-dA/dt - time from the Q wave of the ECG to the peak of dA/dt
dA/dt(max) - the maximum rate of rise of the ACG

Systolic time intervals

QS - total electromechanical systole
LVET - left ventricular ejection time
PEP - pre-ejection period
PEP/LVET - the ratio of PEP to LVET

S V - stroke volume
C A P - carotid arterial pressure

Time constant - a condenser and a resistor in series have a characteristic time constant which expressed in seconds is equal to the product of the capacitance of the condenser (in farads) and the resistance of the resistor (in ohms). By definition, in a circuit with time constant 1 sec., the reproduced square wave will have fallen $1/e$ or 0.37 of its original amplitude in 1 sec.

Frequency response - the variation in sensitivity over the frequency range of the measurement.

Linearity - the degree to which variations in output of an instrument follows input variations.

Echocardiography

A - mode - amplitude - modulated display
B - mode - brightness or intensity-modulated display
M - mode - method of data presentation used in B-mode where the trace is moved across the oscilloscope while keeping the transducer stationary.
Scans - the transducer is moved, and the trace follows

REFERENCES

- ADOLPH, R J, FOWLER, N O and TANAKA, K (1969) Prolongation of isovolumic contraction time in left bundle branch block. American Heart Journal 78, 585.
- ALPS, B J, CALDER, C, WILSON, A and SCOTT-PARK, F (1983) The beneficial effect of nocardipine on the healing of myocardial infarcts in dogs. Drug Research 33 (11) 12, 1638.
- ARONOW, W S, KAPLAN, M A and ELLISTAD, M (1969) Prediction of left ventricular contractility in mitral valve disease by EICT and LVET/EICT measurements. Clinical Research 17, 226.
- BENCHIMOL, ALBERTO and DIMOND, E GRAY (1963) The normal and abnormal apexcardiogram. Its physiologic variation and its relation to intracardiac events. American Journal of Cardiology 12, 368.
- BENCHIMOL, A, DIMOND, E G and CARSON, J C (1961) The value of the apexcardiogram as a reference tracing in phonocardiography. American Heart Journal 61, 485.
- BENCHIMOL, A, DIMOND, E G and SHEN, Y (1960) Ejection time in aortic stenosis and mitral stenosis. American Journal of Cardiology 5, 728.
- BENCHIMOL, A, WU, TEH-LU and DIMOND, E G (1966) Apex cardiogram in the diagnosis of congenital heart disease. American Journal of Cardiology 17, 63.
- BOON, J, WINGFIELD, W E and MILLER, C W (1983) Echocardiographic indices in the normal dog. Veterinary Radiology 24, 214.
- BUSH, C A, LEWIS, R P, LEIGHTON, R F, FONTANA, M E and WEISSLER, A M (1970) Verification of systolic time intervals and the true isovolumic contraction time for the apexcardiogram by micro-manometer catheterisation of the left ventricle and aorta. Circulation (ABSTR) 42, 121.
- COGHLAN, C, PRIETO, G and HARRISON, T R (1961) Movement of the heart during the period between the onset of ventricular excitation and the start of left ventricular ejection. American Heart Journal 62, 65.
- COULSHED, N and EPSTEIN, E J (1963) The Apexcardiogram: Its normal features explained by those found in heart disease. British Heart Journal 25, 697.
- CRAIGE, E (1971) Clinical value of apex cardiography. American Journal of Cardiology 28, 118.
- CRAIGE, E (1975) The value of apexcardiography in cardiac diagnosis. Cardiovascular Clinics 6, 179.
- CREHORE, A C (1911) A study of tracings from the region near the apex of the heart. Journal of Experimental Medicine 14, 351.
- CROMWELL, L, WEIBELLS, S J, PFAIFFER, E A and USSELMAN, L B (1973) IN Biomedical instrumentation and measurement. Prentice Hall Inc. New Jersey.
- DARKE, P G G (1979) Cardiovascular System IN Canine Medicine and Therapeutics. 1st edn p 1. Blackwell Scientific Publications.
- DELIYANNIS, A A, GILLAM, P M S, MOUNSEY, J P D and STEINER, R E (1964) The cardiac impulse and motion of the heart. British Heart Journal 26, 396.

- DENEF, B, DE GEEST, H and KESTELOOT, H (1973) Influence of changes on myocardial contractility on the height and slope of the calibrated apex cardiogram. American Journal of Cardiology 32, 662.
- DENEF, B, VAN DE WERF, F, DE GEEST, H and KESTELOOT, H (1976) Calibrated apexcardiography and assessment of left ventricular dynamics in man. European Journal of Cardiology 4, 143.
- DENEF, B, POPEYE, R, DE GEEST, H and KESTELOOT, H (1975) On the value of calibrated displacement apexcardiography. Circulation 51, 541.
- DIMOND, E G, DUENAS, A and BENCHIMOL, A (1966) Apex Cardiography. American Heart Journal 72, 124.
- EDDLEMAN, E E HEFNER, L, REEVES, T J and HARRISON, T R (1957) Movements and forces of the human heart. 1 The genesis of the apical impulses. A.M.A. Archives of Internal Medicine 99, 401.
- EDDLEMAN, E E, WILLIS, K, CHRISTIANSON, L, PIERCE, J R and WALKER, R P (1953) The kinetocardiogram. II The normal configuration and amplitude. Circulation 8, 370.
- EDDLEMAN, E E, WILLIS, K REEVES, T J and HARRISON, T R (1953) The kinetocardiogram. 1 Method of recording precordial movements. Circulation 8, 269.
- FRANK, O (1959) On the dynamics of cardiac muscle. American Heart Journal 58, 282.
- GABOR, G, PORUBSZKY, I and KALMAN, P (1972) Determination of systolic time intervals using the apex cardiogram and its first derivative. American Journal of Cardiology 30, 217.
- GARRARD, C L, WEISSLER, A M and DODGE, H T (1970) The relationship of alterations in systolic time intervals to ejection fraction in patients with cardiac disease. Circulation 42, 455.
- GARROD, A H (1874-75) On some points connected with circulation of the blood arrived at from a study of the sphygmograph. Proceedings of the Royal Society of London 23, 140.
- GAY, C C, McCARTHY, M CARTER, J and REYNOLDS, W T (1978) Relationship between apex cardiogram and left ventricular pressure events in greyhound dogs. American Journal of Veterinary Research 39, 1322.
- GORDON, J W (1877) On certain molar movements of the human body produced by circulation. J Anat Physiol 11, 533.
- American Heart Journal 68, 220.
- GROSS, D R, PIPERS, F S and HAMLIN, R L (1974) Normal Systolic time intervals in awake dogs and their response to digitalis glycosides. American Journal of Veterinary Research 35, 15.
- HARVEY, W (1628; IN Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus. Frankfurt.
- HAMLIN, R L, OLSEN, I SMITH, C R and BOGGS, S (1967) Clinical relevancy of heart rate in the dog. Journal of the American Veterinary Medical Association 151, 60.
- HENDERSON, A H (1975) Chapter 7: Contractile basis of heart failure. IN Modern Trends in Cardiology 3, 182.

- HOPE, J (1842) A treatise on the diseases of the heart and great vessels. IN Lea & Blanchard, Philadelphia. 427
- JACKSON, D M (1974) A simple non-invasive technique for measuring cardiac contractility. The Lancet, December 14.
- JAIN, S R and LINDAHL, J (1971) Apexcardiogram and systolic time intervals in acute myocardial infarction. British Heart Journal 33, 578.
- JEZEK, V (1963) Clinical value of the polygraphic tracing in the study of the sequence of events during cardiac contraction. Cardiologia 43, 298.
- JOHNSTON, F D and OVERY, D C (1951) Vibrations of low frequency over the precordium. Circulation 3, 579.
- JOHNSON, J M, SIEGEL, W and BLOMQUIST, G (1971) Characteristics of transducers used for recording the apexcardiogram. Journal of Applied Physiology 31, 796.
- KASTOR, J A ARONOW, S, NAGLE, R E, GARBER, T and WALKER, H (1970) Air leaks as a source of distortion in apexcardiography. Chest 57, 163.
- KATZ, L N (1927) Observations of the dynamics of ventricular contraction in the heart - lung preparations. American Journal of Physiology 80, 470.
- KESTELOOT, H and WILLEMS, J (1967) Relationship between right apexcardiogram and the right ventricular dynamics. Acta Cardiologia 2, 64.
- KITTLESON, M D, EYSTER, G E, KNOWLEN, G G, OLIVIER, N B and ANDERSON, L K (1984) Myocardial function in small dogs with chronic mitral regurgitation and severe congestive heart failure. Journal of the American Veterinary Medical Association 184, 455.
- KREULEN, P H, BOVE, A A, McDONOUGH, M P, SANDS, M J and SPANN, J F (1975) The evaluation of left ventricular function in man. A comparison of methods. Circulation 51, 677.
- LEGLER, J F, BENCHIMOL, A and DIMOND, E G (1963) The apexcardiogram in the study of the 2 OS interval. British Heart Journal 25, 246.
- LEIGHTON, R F, WEISSLER, A M, WEINSTEIN, P B and WOOLEY, C F (1971) Right and left ventricular systolic time intervals. American Journal of Cardiology 27, 66
- LEWIS, R P, BOUDOULAS, H, FORRESTER, W F and WEISSLER, A M (1972) Shortening of electromechanical systole as a manifestation of excessive adrenergic stimulation in acute myocardial infarction. Circulation 46, 856.
- LEWIS, R P, LEIGHTON, R F, FORESTER, W F and WEISSLER, A M (1974) Systolic time intervals. IN Non-invasive Cardiology, 301. ed. Weissler. (New York, Grune and Stratton)
- LEWIS, R P, MARCUS, D R and Garrard, C L (1970) Abnormal systolic time intervals with normal cardiac output in chronic myocardial disease. Circulation (ABSTR) 42 (SUPPL 111): 65
- LEWIS, R P, RITTGERS, S E, FORESTER, W F and BOUDOULAS, H (1977). A critical review of the systolic time intervals. Circulation 56, 146.

- LOMBARD, C W (1984) Echocardiographic and clinical signs of canine dilated cardiomyopathy. *Journal of Small Animal Practice* 25, 59.
- LOMBARD, W P and COPE, O (1926) Duration of the systole of the left ventricle of man. *American Journal of Physiology* 77, 263.
- LUISADA, A A, BHAT, P K and KNIGHTEN, V (1978) The systolic time intervals: A new method of study. *International Symposium, Austria, Boehringer Mannheim. Published 1980.*
- McCONAHAY, D R, MARTIN, C M and CHEITLIN, M D (1972) Resting and exercise systolic time intervals: Correlations with ventricular performance in patients with coronary artery Disease. *Circulation* 45, 592.
- MAHLER, F, ROSS, J, O'ROURKE, R A and COVELL, J W (1975) Effects of changes in preload, afterload and inotropic state on ejection and isovolumic phase measures of contractility in the conscious dog. *American Journal of Cardiology* 35, 626.
- MANOLAS, J, WIRZ, P and RUTISHAUSER (1976) Relationship between duration of systolic upstroke of apexcardiogram and internal indices of myocardial function in man. *American Heart Journal* 91, 726.
- MAREY, E J, LEDERER, L G and MANDES, J C (1885) *IN* La Methode graphique dans les sciences experimentales. Edition 2, Masson, Paris.
- MARTIN, C E, SHAVER, J A and LEONARD, J J (1972) Physical, signs, apexcardiography, phonocardiography and systolic time intervals in angina pectoris. *Circulation* 46, 1098.
- MARTIN, C E, SHAVER, J A, THOMPSON, M E, REDDY, P S and LEONARD, J J (1971) Direct correlation of external systolic time intervals with internal indices of left ventricular function in man. *Circulation* 44, 419.
- MASHIMO, K, TANABE, Y, KINOSHITA, S, SAKAMOTO, S and Tsaushima, N (1966) An instrumental aspect of apexcardiography decay characteristics of transducers and its clinical implications. *Japanese Heart Journal* 7, 536.
- METZGER, C C, CHOUGH, C B, KROETZ, F W and LEONARD, J J (1970) True isovolumic contraction time: Its correlation with two external indexes of ventricular performance. *American Journal of Cardiology* 25, 434.
- MILLER, M E (1964) *IN* Anatomy of the dog. W B Saunders.
- MOUNSEY, P (1959) Praecordial pulsations in relation to cardiac movement and sounds. *British Heart Journal* 21, 457.
- MUIR, W W and HAMLIN, R L (1973) Respiratory fluctuations in durations of phases of ventricular systole in the dog. *American Journal of Veterinary Research* 34, 647.
- MYER, C W and BONAGURA, J D (1982) Survey radiography of the heart. *Veterinary Clinics of North American* 12 (2), 213.

- ORESHKOV, V (1965) Indirect measurement of isovolumetric contraction time on the basis of polygraphic tracing. *Cardiologia* 47, 315.
- PARKER J L, and ADAMS, H R (1978) The influence of chemical restraining agents on cardiovascular function: A review. *Laboratory Animal Science* 28, 575.
- PARRY, C H (1825) Collections from the unpublished medical writings of the late C H Parry. *IN Diseases of the Heart* Volume 2. p111. Underwoods, London.
- PATTERSON, R E, KENT, B B and PEIRCE, E C II (1972) A comparison of empiric contractile indices in intact dogs. *Cardiology* 57, 277.
- PENSINGER, ROBERT R (1968) Chronic congestive heart failure in dogs - Clinical and cathological findings. *Journal of the American Animal Hospital Association* 5, 182.
- PIPERS, F S, ANDRYSCO, R M and HAMLIN, R L (1978) A totally non-invasive method for obtaining systolic time intervals in the dog. *American Journal of Veterinary Research* 39, 1822.
- REALE, A (1967) Evaluation of the contractile state of the human heart from the first derivative of the apexcardiogram. *Circulation* 36, 933.
- RICHMOND, D R, ANGUS, J A, GOODMAN, A H and COBBIN, L B (1975) The effect of heart rate on indices of myocardial contractility in the dog. *Clinical and Experimental Pharmacology and Physiology* 2, 469.
- RIOS, J C and MASSUMI, R A (1965) Correlation between the apex cardiogram and left ventricular pressure. *American Journal of Cardiology* 15, 647.
- ROSS, JOHN, Jnr and PETERSON, KIRK, L (1973) On the assessment of cardiac inotropic state. *Circulation* 47, 435.
- RUSHMER, R F (1976) Functional anatomy and control of the heart. *IN Cardiovascular Dynamics* p76. W B Saunders.
- SHERMAN, J and LEWIS, R P (1972) Systolic time intervals in atrial fibrillation. *Circulation (ABSTER)* 45 & 46 (Suppl II) 220.
- SCHOENFELD, C D, COHEN, S and TAGUCHI, J T (1963) Relationship between cycle length and left ventricular ejection time in atrial fibrillation. *Clinical Research (ABSTR)* 11, 26.
- SISSON, S, and GROSSMAN, J D (1975) *IN the Anatomy of the Domestic animals*. W B Saunders.
- SONNENBLICK, E H (1962) Force-velocity relations in mammalian heart muscle. *American Journal of Physiology* 202, 931.
- SPODICK, D H, and KUMAR, S (1968) Isovolumic contraction period of the left ventricle. *American Heart Journal* 76, 498.
- STEPHALOUROS, M A and WITHAM, A C (1975) Systolic time intervals by echocardiography. *Circulation* 51, 114.
- SULTAN AHMED, S, LEVINSON, G E, SCHWARTZ, C J and ETTINGER, P O (1972) Systolic time intervals as measures of the contractile state of the left ventricular myocardium in man. *Circulation* 46, 559.
- SUTTON, G C, CRAIGE, E and GRIZZLE, J E (1967) Quantitation of precordial movement: II Mitral regurgitation. *Circulation* 35, 483.

- SUTTON, G C, PREWITT, R A and CRAIGE, E (1970) Relationship between quantitated precordial movement and left ventricular function. *Circulation* 41, 179.
- SWINSCOW, T D V (1978) IN Statistics at square one. British Medical Association, London.
- TAFUR, E, COHEN, L S and LEVINE, H D (1964) The normal apex cardiogram. Its temporal relationship to electrical, acoustic and mechanical cardiac events. *Circulation* 30, 381.
- TALLEY, ROBERT C, MEYER, JERRY F and McNAY JOHN L (1971) Evaluation of the pre-ejection period as an estimate of myocardial contractility in dogs. *American Journal of Cardiology* 27, 384.
- TAVEL, M E, CAMPBELL, R W, FEIGENBAUM, H and STEINMETZ, E F (1965) The apex cardiogram and its relationship to haemodynamic events within the left heart. *British Heart Journal* 27, 829.
- TAYLOR, R R, ROSS, J Jnr, COVELL, J W and SONNENBLICK, E H (1967) A quantitative analysis of left ventricular myocardial function in the intact, sedated dog. *Circulation Research* 21, 99.
- THOMAS, W P (1984) Two-dimensional, real-time echocardiography in the dog. *Veterinary Radiology* 25, 50.
- VAN DEN BOS, G C, FLZINGA, G, WESTERHOF, N and NOBLE M N (1973) Problems in the use of indices of myocardial contractility. *Cardiovascular Research* 7, 834.
- VAN DER WERF, F, PIESSENS, J, KESTELOOT, H and DE GEEST, H (1978) Value of apexcardiography for the timing of left ventricular pressure events in man. *Acta Cardiologia* 33, 295.
- VENCO, A, GIBSON, D G and BROWN, D J (1977) Relation between apexcardiogram and changes in left ventricular pressure and dimensions. *British Heart Journal* 39, 117.
- VETTER, W R, SULLIVAN, R W and HYATT, K H (1972) Assessment of quantitative apex cardiography. *American Journal of Cardiology* 29, 667.
- VOIGHT, G C and FREISINGER, G C (1970) The use of apexcardiography in the assessment of left ventricular diastolic pressure. *Circulation* 41, 1015.
- VREDEVOE, L A, CREEKMORE, S P and SCHILLER, N B (1974) The measurement of systolic time intervals by echocardiography, *Journal of Clinical Ultrasound* 2, 99.
- WAAGSTEIN, F HJALMARSON, A C and WASIR, H S (1974) Apexcardiogram and systolic time intervals in acute myocardial infarction and effects of practolol. *British Heart Journal* 36, 1109.
- WALLACE, A G, MITCHELL, J H, SKINNER, N S and SARANOFF, S J (1963) Duration of the phases of left ventricular systole. *Circulation Research* 12, 611.
- WEISSLER, A M (1972) Letters to the Editor. Resting and Exercise systolic intervals. *Circulation* 46(3), 633.

- WEISSLER, A M, HARRIS, W S and SCHOENFELD, C D (1968) Systolic time intervals in heart failure in man. *Circulation* 37, 149.
- WEISSLER, A M, HARRIS, W S and SCHOENFELD, C D (1969) Bedside techniques for the evaluation of ventricular function in man. *American Journal of Cardiology* 23, 577.
- WHITSETT, T L, and NAUGHTON, J (1971) Effect of exercise on S T 1 in sedentary and active individuals and rehabilitated patients with heart disease. *American Journal of Cardiology* 27, 352.
- WIGGERS, C J (1921) Studies on the consecutive phases of the cardiac cycle. *American Journal of Physiology* 56, 415.
- WIGGERS, C J (1921) Studies on the consecutive phases of the cardiac cycle II The Laws Governing the relative duration of ventricular systole and diastole.
- WILLEMS, J L, DE GEEST, H and KESTELOOT, H (1971) On the value of apex cardiography for timing intracardiac events. *American Journal of Cardiology* 28, 59.
- WILLEMS, J L, KESTELOOT, H and DE GEEST, H (1972) Influence of acute hemodynamic changes on the apex cardiogram in dogs. *American Journal of Cardiology* 29, 504.
- WINGFIELD, W E, BOON, J and MILLER, C W (1982) Echocardiographic assessment of mitral valve motion, cardiac structures, and ventricular function in dogs with atrial fibrillation. *Journal of the American Veterinary Medical Association* 181, 46.